
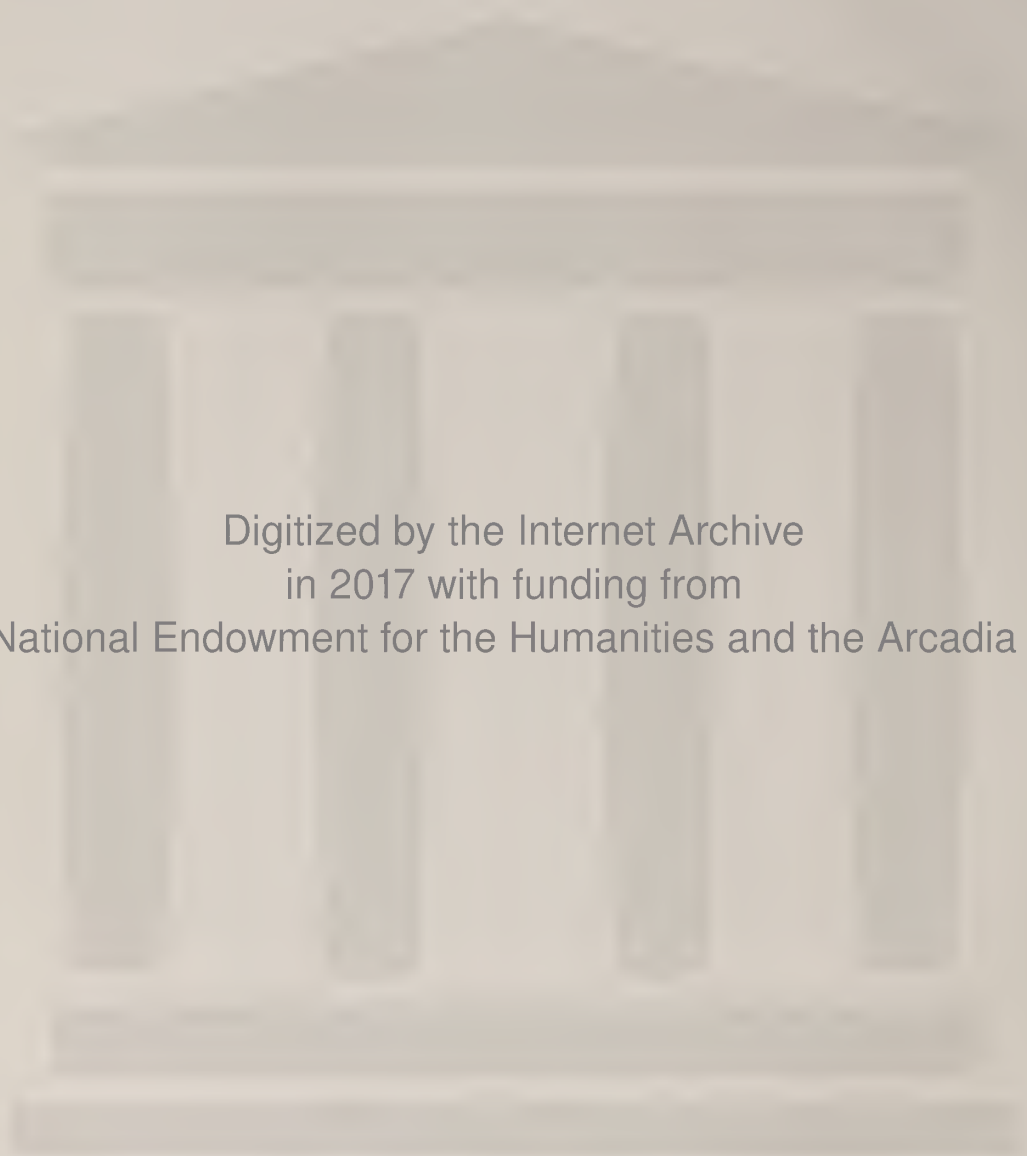


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BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

ACUTE OLIGURIC RENAL FAILURE ASSOCIATED WITH
LOW-MOLECULAR-WEIGHT DEXTRAN 1

Rafael Burgos-Calderón, MD and Julio E. Figueroa, MD

TREATMENT OF SCHISTOSOMIASIS MANSONI IN ADULTS
WITH SODIUM DIMETHYLCYSTEINE TARTRATE 5

Federico Hernández Morales, MD and José Oliver-González, MD

IMPRESIONES DERMOPAPILARES: DERMATOGLIFICOS Y SURCOS
DE FLEXION – I. CONCEPTOS BASICOS 8

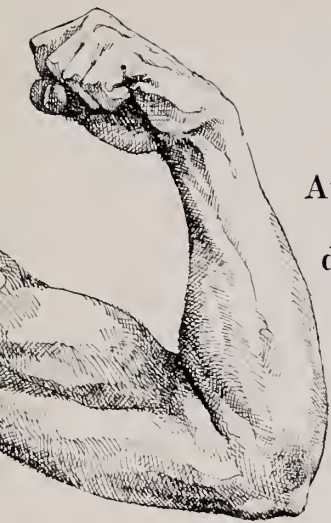
Adolfo Pérez-Comas, MD and José Miguel García Castro, MD

E DITORIAL 14

Dextran 40 – Paradox of Treatment

NOTICIAS 15

IF MORE MEN CRIED



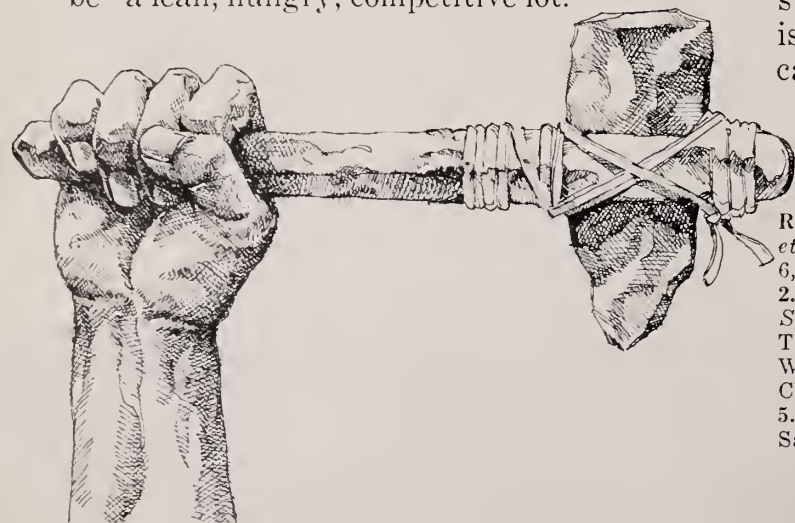
At least seventy-five out of one hundred adults with duodenal ulcers are men.¹

Why? It may be significant that duodenal ulcer patients tend to crave recognition and are "especially vulnerable to threats to their manly assertive independence."²

Hypersecretion—an atavistic response.

Stewart Wolf, who, with Harold G. Wolff, studied the personalities of duodenal ulcer patients, wonders if masculine competitiveness is related to "an atavistic urge to devour an adversary." It is striking, he reports, that an accentuation of gastric acid secretion and motility can be "induced in ulcer patients by discussions that arouse feelings of inadequacy, frustration and resentment."²

By chance? A lean, hungry lot. Was the link between emotions and gastric hyperacidity acquired through mutation to serve a purpose? During man's jungle period of evolution, the investigator points out, a male dealt with a foe by killing and devouring it. "It may be more than coincidence," he concludes, that peptic ulcer patients appear to be "a lean, hungry, competitive lot."³



Big boys don't cry. If more men cried, maybe fewer would wind up with duodenal ulcers. But men will be men—the sum total of

their genes and what they are taught. Schottstaedt observes that when a mother admonishes her son who has hurt himself that big boys don't cry, she is teaching him stoicism.⁴ Crying is the negation of everything society thinks of as manly. A boy starts defending his manhood at an early age.

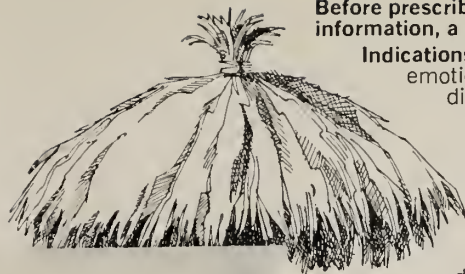


Take away stress, you can take away symptoms.

There is no question that stress plays a role in the etiology of duodenal ulcer. Alvarez⁵ observes that many a man with an ulcer loses his symptoms the day he shuts up the office and starts out on a vacation. The problem is, the type of man likely to have an ulcer is the type least likely to take long vacations or take it easy at work.

The rest cure vs. the two-way action of Librax.[®] For most patients, the rest cure is as unrealistic as it is desirable. Still, the stress factor must be dealt with. And here is where the dual action of adjunctive Librax can help. Librax is the only drug that com-

References: 1. Silen, W.: "Peptic Ulcer," in Wintrobe, M. M., et al. (eds.): *Harrison's Principles of Internal Medicine*, ed. 6, New York, McGraw-Hill Book Company, 1970, p. 1444. 2. Wolf, S., and Goodell, H. (eds.): *Harold G. Wolff's Stress and Disease*, ed. 2, Springfield, Ill., Charles C Thomas, 1968, pp. 68-69. 3. *Ibid.*, p. 257. 4. Schottstaedt, W. W.: *Psychophysiologic Approach in Medical Practice*, Chicago, Ill., The Year Book Publishers, Inc., 1960, p. 163. 5. Alvarez, W. C.: *The Neuroses*, Philadelphia, Pa., W. B. Saunders Company, 1951, p. 384.



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Indicated as adjunctive therapy to control emotional and somatic factors in gastrointestinal disorders.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librax (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, over-sedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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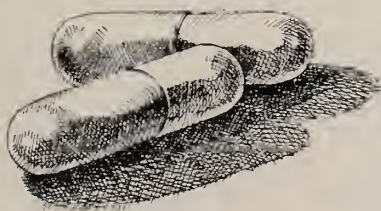
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Warnings: Use during pregnancy is to be avoided.

Precautions: 1. **Starvation Ketosis:** This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria

which, in spite of relatively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.**

2. **Lactic Acidosis:** This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.

3. **Hypoglycemia:** Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin.

Adverse Reactions: Principally gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake.
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have reduced the toll of these age-old threats dramatically. And I see patients in pain from crippling arthritis helped with new medicinals unknown just a few years ago.

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3/29/67 Before therapy with 5%-FU cream. Patient P. T shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

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6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.





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Studies showed that with the 2% and 5% Efudex preparations, the usual duration of therapy was only 2 to 4 weeks.⁵ Other studies with topical fluorouracil revealed that when concentrations of less than 2% were used, significant numbers of lesions recurred.⁶

Treats the lesions you can't see, too.

Numerous lesions, not apparent prior to 2% and 5% Efudex therapy, manifested themselves by definite reactions, while intervening skin remained relatively unaffected.⁵ The early eradication of these subclinical lesions (which may otherwise have undergone further progression) probably accounts for the reduced incidence of future solar keratoses in patients treated with topical fluorouracil—especially with 5% concentrations.⁶

How to identify solar keratoses.

Typically, the lesion—a flat or slightly elevated brown to red-brown papule—is dry, rough, adherent and sharply defined. Multiple lesions are the rule.

Predictable therapeutic response.

The response to a typical course of Efudex therapy is usually characteristic and predictable. After 3 or 4 days of treatment, erythema begins to appear in the area of keratoses. This is followed by a moderate to intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of this response generally occurs two weeks after the start of therapy and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. Lesions that do not respond should be biopsied.

References: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York, Grune & Stratton, 1967, p. 842. 2. Dillaha, C. J.; Jansen, G. T., and Honeycutt, W. M.: "Treatment of Actinic Keratoses with Topical Fluorouracil," in Waisman, M. (ed.): *Pharmaceutical Therapeutics in Dermatology*, Springfield, Ill., Charles C Thomas, 1968, p. 92. 3. Belisario, J. C.: *Cutis*, 6:293, 1970. 4. Sams, W. M.: *Arch. Derm.*, 97:14, 1968. 5. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and Klein, E.: *Cancer*, 25:450, 1970.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

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ACUTE OLIGURIC RENAL FAILURE ASSOCIATED WITH LOW-MOLECULAR-WEIGHT DEXTRAN

Rafael Burgos-Calderón, MD
Julio E. Figueroa, MD

Low-molecular-weight dextran (LMWD) has been used in the treatment of various clinical conditions (1-6). Nevertheless, adverse side-effects can vary from allergic reactions to severe anaphylaxis and acute renal failure. This paper reports a case of acute renal failure associated with LMWD and reviews its role in the pathogenesis of the associated renal failure.

Case Report

A 22-year-old white man was admitted to a hospital in Spanish Honduras, Central America, on July 6, 1968, for treatment of a gunshot injury to the left groin which severed branches of the femoral artery. Cyanosis of the left leg and foot required exploration of the left inguinal area. The left femoral artery was found to be occluded by a thrombus. Thrombectomy and endarterectomy were performed with restoration of circulation. Heparin and 10 percent LMWD (40,000 M.W.; 1000 cc in 24 hours) were given in the immediate post-operative period. The blood pressure was normal throughout. The urinary output was good until the day after surgery when he developed oliguria (60 cc per 24 hours). He was transferred to Ochsner Foundation Hospital 5 days after the injury. Physical findings on admission revealed a blood pressure of 160/80 mm Hg, a pulse of 84/min and regular. Peripheral pulses were present but marked swelling and cyanosis of the left lower extremity was noted. Laboratory studies revealed leukocytosis and anemia. Urinalysis revealed gross hematuria and 4+ albuminuria. The BUN was 150 mg/100 ml; serum creatinine, 12.6 mg/100 ml; serum potassium, 7.2 mEq/liter; and the CO₂ was 16.0 mEq/liter.

Hemodialysis was performed on the day of admission. Inferior vena cavagram revealed non-visualization of the inferior vena cava at the level of L-2. Scintigram utilizing ¹³¹I hippuric acid and ^{99m}Tc pertechnetate study revealed poor function and markedly reduced blood flow to both kidneys. A tentative diagnosis of bilateral renal vein thrombosis was

made. Exploratory laparotomy on July 11, 1968, revealed thrombosis of the left femoral vein but the inferior vena cava and the renal veins were normal. Prophylactic inferior vena caval ligation was done. A renal biopsy at the time of surgery showed marked hydropic degeneration of the proximal convoluted tubules and no evidence of renal arterial or arteriolar disease (Fig. 1). He was maintained on hemodialysis until the diuretic phase ensued—22 days after admission. Percutaneous renal biopsy performed 26 days after admission showed marked improvement (Fig. 2). Upon discharge the endogenous creatinine clearance was 104 ml/min.

Discussion

Typical histologic features of "osmotic nephrosis" following the administration of low-molecular-weight dextran implicates this drug as the etiologic factor in the pathogenesis of acute renal failure in the patient described above. Other factors such as shock, vaso-pressors, and renal vein thrombosis were ruled out. The effect of trauma and surgery on the renal function cannot be discarded. Review of the literature (Table I) reveals that the correlation between LMWD administration and acute renal failure is greater in older patients, in patients with pre-existing renal disease with azotemia, and peripheral vascular disease. None of these problems was present in the patient described.

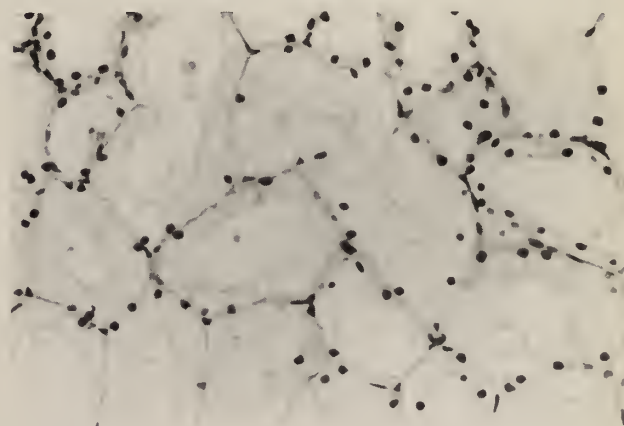


Fig. 1: Photomicrograph showing marked hydropic tubular cell degeneration compatible with osmotic nephropathy.

From the Department of Internal Medicine, Section of Nephrology, Louisiana State University School of Medicine New Orleans, and Alton Ochsner Medical Foundation, New Orleans, and from the Dialysis and Renal Transplantation Program, Ochsner Medical Center, New Orleans, Louisiana.

Reprint requests to Alton Ochsner Medical Foundation, 1514 Jefferson Highway, New Orleans, Louisiana 70121.

TABLE I: CASES REPORTED IN THE LITERATURE OF THE ASSOCIATION OF
INFUSION OF LMWD AND ACUTE RENAL FAILURE

Author and Reference	Year	No. Cases	Age in Years	Diagnosis or Associated Condition	Outcome
Almgard et al (19)	1965	1	22	Burned with high alternating current; Severe dehydration	Survived
Langsjoen (20)	1965	6	?	Pre-existing renal disease	Died
Goodwin et al (21)	1965	1	56	Left atrial myxoma, multiple embolization	Died
Wilkenson (22)	1965	3	95	Severe hypotension	Died
			?	Crush injury of right leg	Died
			?	Lumbar sympathectomy in peripheral vascular disease	Died
Morgan et al (23)	1966	3	77	Acute popliteal artery obstruction	Died
			67	Myocardial infarct, ischemic I. hand	Survived
			58	Radionecrotic ulcer	Survived
Daniel et al (24)	1966	1	71	Myocardial infarct, pulmonary embolism, mesenteric embolism	Survived
Niall and Doyle (25)	1966	3	?	Aorto-femoral bypass	?
				Common iliac occlusion	?
Hulme and Lawson (26)	1966	2	?	Vascular surgery	?
Evans and Wong (27)	1966	1	74	Occlusion left femoral artery; hypertensive nephrosclerosis	Died
Fillastre et al (28)	1967	1	68	Acute femoral ischemia	Survived

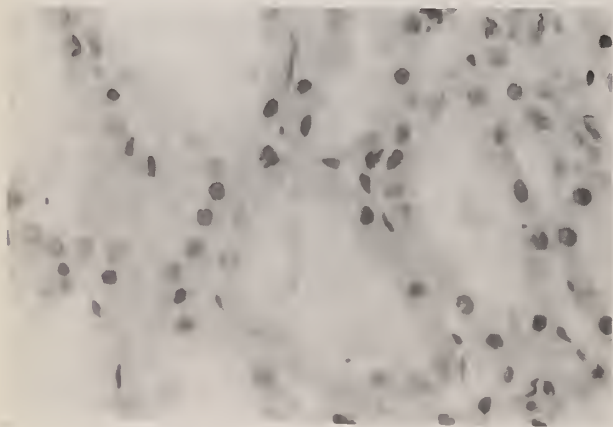


Fig. 2: Photomicrograph obtained during recovery phase revealing near normal tubular architecture.

Great controversy has existed since the term "osmotic nephrosis" was coined by Allen (8) to describe the marked swelling and vacuolization of proximal tubular cells associated with the administration of dextran, mannitol, and hypertonic glucose. Several investigators have shown that in dehydrated states, LMWD is concentrated in the proximal tubules producing a viscous fluid which could result in tubular obstruction. Hendren (9) found hydropic degenerative changes in the renal tubules in dogs given LMWD before or after a period of renal artery occlusion. Electron microscopic studies in mice by Engberg and Ericsson (10) showed that the proximal tubule vacuolization is due to enlargement of lysosomes and the occurrence of increased numbers of endocytic vacuoles. In this study both endocytic vacuoles and enlarged lysosomes were presumed

to contain reabsorbed dextran.

In contrast, Mailloux *et al* (11) found no evidence of either tubular vacuolization or hydropic degeneration after the infusion of LMWD in dogs with unilateral stenosis of the renal artery. Nevertheless they found stainable dextran in Bowman's space and in the renal tubules. They explained the lack of findings on the basis of the acuteness of their experiments.

The functional significance of these changes continues to be a matter of debate. Goldenberg *et al* (12) were unable to demonstrate any changes in urea clearances, in non protein nitrogen and alkaline phosphatase. Studies by Klutsch *et al* (13) in normal individuals failed to reveal any marked changes in renal function. Matheson (14) gave large doses of LMWD to hydropenic individuals and found no changes in the excretory index of renal tubular cells. Studies in animals have shown similar results (15).

Although the mechanism by which LMWD could produce renal failure or deteriorate renal function remains unclear, the following factors have been considered important:

1. There is evidence that LMWD can produce anaphylaxis in man (16).
2. It is known that histamine, released by dextran (75,000), will decrease renal perfusion pressure. This phenomenon has not yet been described by LMWD (17).
3. It has been shown that LMWD produces shunting of blood from cortex to medulla (18).
4. It has been shown that plugging of the renal tubules with dextran can produce tubular obstruction; nevertheless, there are many reports in the literature in which renal failure was not associated with tubular obstruction.
5. The role of renal hypoperfusion in combination with tubular obstruction was put forward by Mailloux *et al* (11) on the basis of experiments in dogs.
6. Since LMWD has been identified inside the renal tubular cells, the possibility exists that it could produce metabolic alterations in the proximal tubular cells interfering with active transport. This concept has received support from the work of Engberg and Ericsson (10).

Recently Pollack and Kark (7) have reported an entirely different pathologic entity—acute glomerulonephritis—to be associated with the administration of dextran. Light microscopy reveals proliferative changes and electron microscopy shows epithelial humps. No tubular changes were associated with this lesion. The pathogenesis of this entity appears to be mediated through a hypersensitivity phenomenon.

The cause and effect relationship of LMWD and

acute renal failure remains unsettled. It is, however, of great importance for the clinician to be aware of the possibilities of development of either osmotic nephropathy or acute hypersensitivity glomerulonephritis whenever this drug is used. Caution is therefore imperative and the beneficial effects of this drug must be always weighed against the possibility of the complications of its use.

Summary

Low-molecular-weight dextran, although useful in the treatment of a variety of clinical conditions, may have adverse side-effects varying from allergic reactions to severe anaphylaxis and acute renal failure. A 22-year-old white man required thrombectomy and endarterectomy for a gunshot wound in the left groin. After receiving 1000 cc of dextran in 24 hours, he developed oliguria and required hemodialysis. He was maintained on hemodialysis for 22 days until the diuretic phase ensued. He subsequently recovered.

Experimental evidence linking low-molecular-weight dextran to "osmotic nephrosis" has been equivocal. Several investigators have shown that in dehydrated states, LMWD is concentrated in the proximal tubules producing a viscid fluid which could result in tubular obstruction. Other investigators have found no evidence of either tubular vacuolization or hydropic degeneration after the infusion of LMWD in dogs. Acute hypersensitivity glomerulonephritis has also reportedly occurred after the administration of LMWD. Although the cause and effect relationship of LMWD and acute renal failure is still obscure, indiscriminate use of the drug is not justified.

Resumen

A pesar de la utilidad de DEXTRAN, de bajo peso molecular, en una variedad de condiciones clínicas, esta droga puede tener efectos adversos de gran seriedad. Estos efectos pueden variar entre anafilaxis severa y anormalidades renales, tales como glomerulonefritis aguda o fallo renal agudo debido a necrosis tubular. Un joven de veintidós años, que requirió trombectomía y endarterectomía en la región femoral derecha, debido a un accidente, desarrolló fallo renal agudo después de hacerse infusión con DEXTRAN de peso molecular bajo. El paciente requirió diálisis, pero recobró función renal después de fase diurética, veintidós días más tarde. Biopsias renales durante la fase

oligúrica y en la fase diurética demostraron cambios típicos de nefrosis osmótica con recuperación en la fase diurética.

La evidencia experimental conectando el DEXTRAN de peso molecular bajo a la llamada nefrosis osmótica no está completamente aclarada. Varios investigadores han demostrado que en condiciones de deshidratación, DEXTRAN de peso molecular bajo es concentrado por los túbulos proximales, produciendo un líquido viscoso que podría producir obstrucción tubular. Otros investigadores no han encontrado evidencia de vacuolización tubular o cambios hidrópicos, después de la infusión de esta droga en perros. Sin embargo, glomerulonefritis, probablemente por hipersensitividad a la droga, ha sido reportada en la literatura médica, así como fallo renal agudo asociado con la misma droga. A pesar de que la relación de causa-efecto entre DEXTRAN de peso molecular bajo y los cambios fisiológicos renales, no está completamente aclarada es recomendable usar dicha droga con gran cuidado teniendo en mente la posibilidad de daño renal.

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TREATMENT OF SCHISTOSOMIASIS MANSONI IN ADULTS WITH SODIUM DIMETHYL-CYSTEINE TARTRATE

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Sodium antimony-dimethylcysteine tartrate (NaP) is a crystalline water-soluble compound with a total antimony content of 14.5 percent after mixture of 5.8 parts sodium antimony tartrate and 10 parts d I - penicillamine for proper development (1, 2, 3). Penicillamine, a surface containing amino-acid has been shown by many authors to promote detoxification of various metal ions probably by virtue of its chelating properties. It lowers the acute toxicity of tartar emetic for hamsters and white mice infected with *S. mansoni*, without affecting the host tissue-antimony levels; an antimony penicillamine couple is formed which is less toxic to the host, but still as parasitocidal to the schistosome as the tartar emetic alone (4, 5).

Clinical trials with NaP were conducted by Ron Pedrique *et al*, in 108 individuals, aged 15 to 62 years, and proven infected with *S. mansoni* by the presence of ova in the stools (6). One daily injection for five consecutive days was administered deep into the gluteal region, the total dose received was 2 gms. corresponding to 290 mg. of antimony per individual. Out of the 108 patients who started therapy, 104 completed the full schedule of five injections.

Drug intolerance was manifested more frequently during the first and second day of treatment. The main side reactions were nausea, vomiting and vertigo, with slight fever and diarrhea. These were observed in 45 (44.4 percent) out of the 108 patients. Three patients abandoned therapy after the first injection which was followed by nausea, vomiting, vertigo, and did not return. The remaining 105 patients, completed the full schedule.

In our study the compound was administered to a group of twelve adult male inmates, aged 20 to 33 years, from a local penitentiary at the dose of 400 mg. daily

given intramuscularly for five days to a total of 2 gms. The patients were mostly asymptomatic, passing numerous eggs of *Schistosoma mansoni*. Another group of 4 inmates, aged 22 to 27 years, received injections of saline as a placebo. All of the individuals injected were observed for side reactions, and laboratory examinations consisted of complete blood counts, liver function tests (Hanger, SGO-T, SGP-T) and BUN. Urine samples were tested for albumin, glucose, bile, and urobilinogen. Electrocardiograms were taken before and after therapy.

Fecal examinations were performed at regular intervals during and after therapy using the Ritchie's formol ether technique for counting eggs, except that the entire sediment was examined and eggs counted.

Results

Side reactions — consisted chiefly of nausea and vomiting in 5 (41.6 percent) of the twelve patients during the five days of therapy, but which ceased after therapy. One patient developed joint pains and another an epileptic seizure for one day which later disappeared. No side reactions were observed in the patients treated with placebo.

In all cases which received the drug, the SGO-T and SGP-T values were found elevated on the 4th and 8th day after onset of therapy. Urobilinogen was increased in 6 out of the 12 cases (Table I). The remaining blood and urine determinations such as complete blood counts, Hanger's test, BUN and albumin, glucose and bile tests, were within normal limits.

Results of egg counts in the treated patients are presented in Table II. These were markedly reduced as compared with pre-treatment levels on the 10th day after therapy and negative on the 60 and 90th day of follow-up. The egg counts of stools from patients administered placebo were still positive on the 90th day with no significant reductions.

Electrocardiograms were taken prior to and 8 to 9 days after treatment was started. Minor T-wave chan-

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TABLE I: BLOOD AND URINE TESTS BEFORE AND ON THE 4TH AND 8TH DAY AFTER ONSET OF THERAPY

Case No.	SGO-T			SGP-T			Urobilinogen
	Before	4th	8th	Before	4th	8th	8th Day
1	21	30	46	17	32	42	Increased
2	35	36	62	25	52	56	Normal
3	36	58	94	30	56	104	Increased
4	46	84	140	38	47	140	Normal
5	50	132	131	47	120	132	Increased
6	16	36	69	10	20	52	Normal
7	18	54	102	23	47	132	Increased
8	102	92	150	88	128	150	Normal
9	28	66	74	30	42	88	Normal
10	26	52	40	52	110	58	Increased
11	23	46	74	23	52	70	Normal
12	32	40	64	26	26	47	Increased

TABLE II: EGGS OF *SCHISTOSOMA MANSONI* PER GRAM OF FECES BEFORE AND AFTER TREATMENT WITH NAP

Case	Number	Pre-therapy counts; average for three consecutive days	Follow up counts: Days after drug administration		
			10	60	90
1		29	1	0	0
2		44	2	0	0
3		23	15	0	0
4		36	1	0	0
5		25	2	0	0
6		10	0	0	0
7		9	0	0	0
8		10	0	0	0
9		10	0	0	0
10		18	1	0	0
11		16	1	0	0
12		37	0	0	0
		Placebo			
1		12	4	12	11
2		25	6	6	8
3		12	6	7	8
4		29	23	10	13

ges were observed in 2 of the treated patients. Prominent T-wave-ischemic-changes were observed in the first 3 precordial leads in one. There were no alterations in rhythm, R-R or Q.R.S. intervals.

Discussion and Summary

Sodium antimony-dimethylcysteine tartrate (NaP) was tested on twelve patients 20 to 33 years old, passing eggs of *Schistosoma mansoni* at a dose of 400 mg. daily for five days. The drug had a marked and quick effect since in all twelve patients the stools had low or negative counts beginning on the 10th day, and all became negative on the 60 and 90 days after therapy. This agrees with the findings of Ron Pedrique, *et al* (6), in *S. mansoni* infections, and Santos (7), in *S. japonicum* infections, in which cure rates were above 90.0 percent in patients observed for three months.

Side reactions consisting of nausea and vomiting were observed in 5 out of the 12 treated patients during the first two days of therapy, but ceased thereafter. Blood tests for SGO-T and SGP-T revealed elevated values, which are usually observed during therapy with antimonials, which later returned to normal.

Although the number of cases used in this study is relatively small, the drug shows promise for the treatment of schistosomiasis. According to Ron Pe-

drique (6), the doses used so far are possibly above the minimal required for effectiveness, and thus the smallest effective antimony amount required needs further evaluation.

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IMPRESIONES DERMOPAPILARES: DERMATOGLÍFICOS Y SURCOS DE FLEXIÓN I. CONCEPTOS BÁSICOS

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El estudio de las líneas dermopapilares (puntas de los dedos, palmas de las manos, plantas de los pies) sirven de gran ayuda al clínico para la orientación diagnóstica de múltiples afecciones cromosómicas y hereditarias. De antaño, los quirománticos han empleado el estudio de los pliegues palmares para sus predicciones. Ejemplos muy antiguos del empleo de las huellas digitales para la identificación personal pueden encontrarse en antiguos documentos chinos. Galton (1), en 1892, estableció los patrones dermopapilares de los dedos, basándose en sus estudios y en los previos realizados por Herschel (2) y Faulds (3), comenzando así su empleo en la identificación policial. En el año 1936, Cummins (4) estableció el significado de los patrones dermopapilares en el mongolismo, lo cual ha sido confirmado por múltiples autores. Posteriormente, se han encontrado patrones más o menos característicos en otras afecciones cromosómicas y hereditarias, como son: los síndromes de Klinefelter, Turner, Rubinstein-Taybi, trisomías 13 y 18, diversas cardiopatías congénitas, embriopatía rubélica, talasemia, esquizofrenia y fenilcetonuria entre otras.

Los pliegues cutáneos se desarrollan en relación con los cojinetes volares. Durante la decimotercera semana de gestación comienzan a aparecer completándose su desarrollo al momento del nacimiento en el niño a término. Una vez formados se mantienen de forma idéntica toda la vida, excepto por su tamaño. Aunque no de forma definida, se cree que los surcos de flexión son secundarios a la plegadura de la mano embrionaria. Por

ende, cualquier condición que afecte el desarrollo embrionario en este período puede manifestarse en alteraciones de los dermatoglíficos.

Dada su importancia en la medicina clínica, nos proponemos exponer, a grandes rasgos, los puntos sobresalientes en el estudio de las impresiones dermopapilares y las correlaciones clínicas pertinentes. Serán temas de comunicaciones posteriores los valores normales para Puerto Rico y las características especiales de diversas afecciones cromosómicas y hereditarias.

Métodos de estudio de las impresiones dermopapilares:

El estudio puede ser realizado por varios métodos, simples en su mayoría, como es la inspección mediante una lupa, o mediante la impresión de las huellas sobre papeles simples o especiales empleando diversas técnicas, que varían desde el método sencillo de la almohadilla entintada y papel corriente hasta el empleo de una solución sensibilizadora incolora y papel especial*. Este método no ensucia las manos ni el área examinada, y, a nuestro parecer, resulta ser el mejor.

Conceptos Básicos:

La nomenclatura empleada en la descripción de las impresiones dermopapilares fue establecida en el simposio auspiciado por la fundación Ciba en 1967 (5).

1. Impresiones dactilares:

a. Patrones:

Existen cuatro patrones básicos, a saber, arco, arco en tienda (o entoldado), bucle y torbellino (o espiral). El tipo de patrón dependerá del número de trirradios presentes. Se define un trirradio como el punto de unión de tres líneas dérmicas, cuyos ángulos de intersección son superiores a 90° (figura 1).

El arco es un sistema curvo de pliegues sin un patrón verdadero con la convexidad dirigida hacia la punta del dedo. En este patrón no existen trirradios, solo hay una disposición de líneas paralelas (figura 2a).

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* Faurot, Inc., 299 Broadway, New York 7, N. Y.

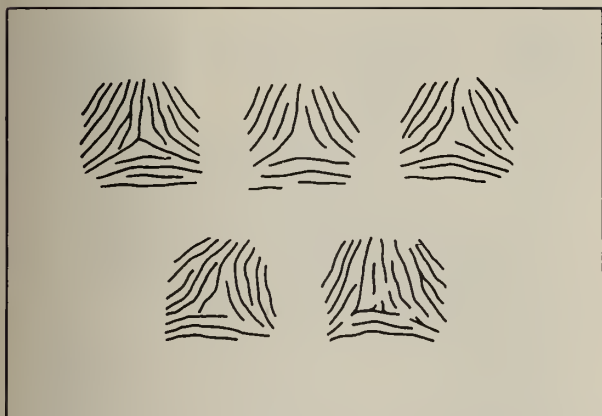


Fig. 1: Diversos tipos de trirradio.

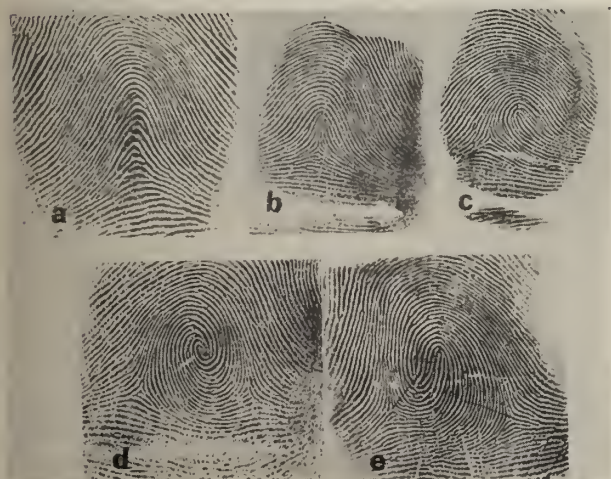


Fig. 2: Patrones básicos: a. arco; b. arco en tienda; c. bucle; d. torbellino o espiral; e. espiral bucle doble.

El arco en tienda o entoldado es un arco muy estrecho que parece tener un trirradio en posición central, aunque técnicamente no lo es al estar constituido por la unión de dos sistemas dérmicos (figura 2b).

El bucle o asa es un patrón dérmico con un solo trirradio que abre hacia uno de los lados del dedo. Según abra en sentido radial o cubital recibe el nombre de bucle radial o cubital (figura 2c). Su configuración puede variar considerablemente, presentando una abertura ancha o bien estrecha.

El torbellino o espiral representa un patrón dérmico comprendido entre dos trirradios. La configuración del patrón varía desde un espiral más o menos concéntrico hasta un bucle doble (figura 2d y 2e, respectivamente).

Para fines prácticos, estos patrones se pueden esquematizar de la forma en que se ilustra en la figura 3.

El valor del estudio de los patrones estriba en que en individuos normales algunos son más frecuentes que otros. Si consideramos las características digitales de ambas manos, en total diez, y examinamos su frecuencia en una población blanca, encontraremos que los bucles constituyen el 70 por ciento de las impresiones, los torbellinos un 25 por ciento y los arcos un 5 por ciento (6).

Los bucles cubitales son once veces más frecuentes que los radiales, mientras que los arcos son siete veces más frecuentes que los arcos en tienda. Cabe señalar que cada dedo presenta una frecuencia particular de patrón. Así, por ejemplo, los bucles digitales tienen una frecuencia que oscila entre el 85 por ciento para el dedo meñique (V) y el 34 por ciento para el índice (II). Los torbellinos, menos frecuentes que los bucles, se encuentran en un 42 por ciento en el dedo anular (IV), 35 por ciento en el pulgar (I) y en un 18 y 13 por ciento en los dedos medio (III) y meñique (V), respectivamente (6). Igualmente existen diferencias entre las dos manos. Si

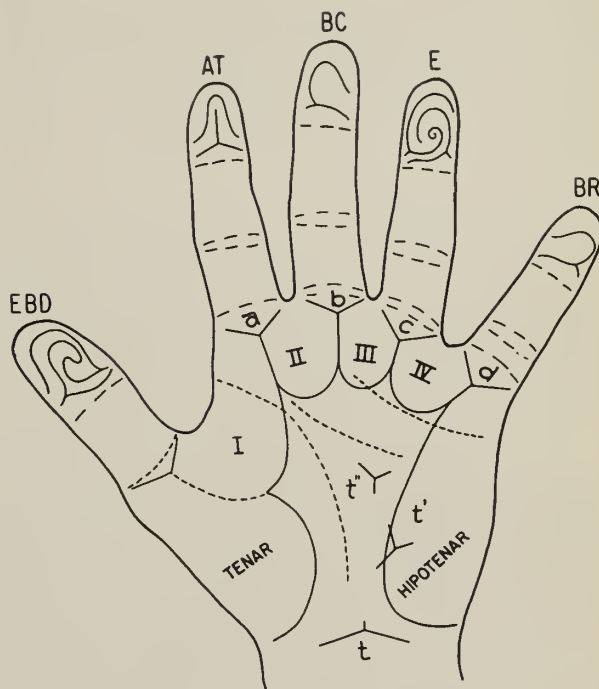


Fig. 3: Diagrama de la mano que muestra trirradios palmares, áreas interdigitales y patrones digitales.

bien son frecuentes los torbellinos en el pulgar, recurren aún más a menudo en el de la mano derecha que en el de la izquierda (39 y 31 por ciento, respectivamente) (6). Dado el hecho de que las frecuencias de estos patrones pueden variar con la población, cabría esperar algunas diferencias en Puerto Rico. Estos resultados serán el tema de una próxima comunicación. Apuntemos que en algunas afecciones cromosómicas y hereditarias esta frecuencia se encuentra alterada de una forma característica.

2. Impresiones palmares:

En la palma de la mano debemos señalar la presencia o ausencia de patrones en las áreas tenar, hipotenar e interdigitales, y la posición relativa del trirradio axial. También se debe estudiar la morfología de los surcos de flexión.

a. Patrones palmares:

En la palma de la mano pueden haber patrones básicos como en los dedos, vestigios—patrones incompletos—, o un “campo abierto”, es decir, la ausencia de patrones específicos.

b. Trirradios digitales:

Los trirradios digitales son usualmente cuatro, estando por lo general situados en las bases de los dedos II, III, IV, y V. Se conocen como a, b, c, y d, respectivamente (figura 3). Ocasionalmente, un trirradio digital se encuentra ausente, ocurriendo entonces el que un solo trirradio interdigital sostiene dos dedos. Si dicho trirradio se encuentra situado en posición central entre dos dedos (como ocurre en la sindactilia) se puede llamar bc o cd.

c. Trirradio axial:

En la palma de la mano se encuentra un trirradio axial cerca del surco de flexión de la muñeca, situado centralmente, aunque en ocasiones hallamos más de un trirradio axial. Cuando esto ocurre, debemos valorar al trirradio más distal como el de mayor importancia para el análisis clínico. Este trirradio axial recibe el nombre de “t”.

La posición del trirradio axial se puede expresar de tres maneras distintas. Penrose (7-8), propuso en el 1949 la medida del ángulo atd, el cual estaría formado por las líneas que unen los trirradios de la base de los dedos índice y meñique con el trirradio axial (figura 4). Mientras más distal esté el trirradio, mayor será el ángulo. Todo ángulo superior a los 57° se considera distal.

También puede determinarse como la relación (en tanto por ciento) entre la distancia del trirradio “t” al surco de flexión más proximal del tercer dedo con la distancia palmar, medida entre el surco de flexión más



Fig. 4: Medida del ángulo atd en mano izquierda: 54° en este ejemplo. Valor normal menor de 57° .

distal de la muñeca y el surco de flexión más proximal del tercer dedo. Walker (8-9), propone como normal todo valor inferior o igual a 39 por ciento. Todo valor igual o mayor al 40 por ciento implica la presencia de un trirradio axial distal o alto. En ocasiones los valores se expresan como t si varía entre 0-14 por ciento, t' entre 15-39 por ciento y t'' si es superior al 40 por ciento (figura 5).

Una tercera forma de expresar la posición del trirradio axial lo constituye el recuento de pliegues entre el trirradio d y el trirradio hipotenar más distal. Este valor será menor cuando “t” esté colocado en posición distal. Este método tiene la ventaja de que no varía con la edad, pero presenta la gran desventaja que conlleva el contar el número de pliegues de un área tan amplia, lo cual no resulta fácil con la inspección directa, ni aún con las impresiones en papel.

En los niños, es preferible emplear la forma de porcentajes ya que la mano se alarga con el crecimiento, variando el valor del ángulo atd. Un error posible al medir el ángulo atd estriba en que su valor puede variar según la persona coloque sus dedos juntos o separados al hacer la impresión sobre el papel, llegando inclu-

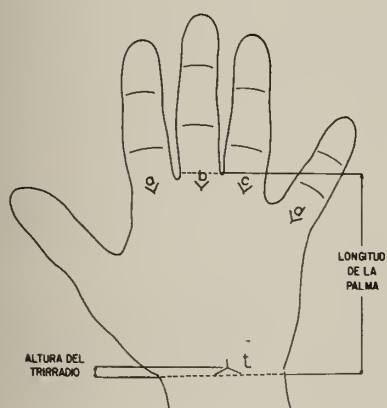


Fig. 5: Posición del trirradio. Determinado a partir de la altura del trirradio. Valor normal: menor de 40 por ciento.

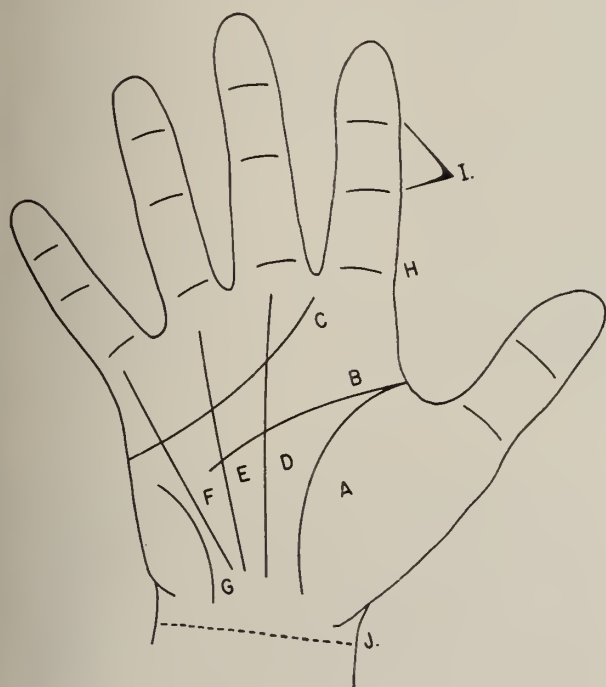


Fig. 6: Surcos de flexión más comunes de la mano. A. Surco tenar (surco longitudinal radial, "vida"); B. surco transversal proximal ("cabeza"); C. surco transversal distal ("corazón"); D. surco del dedo medio; E. surco del cuarto dedo; F. surco del quinto dedo; G. surco hipotenar; H. surcos metacarpofalángicos; I. surcos interfalángicos; J. surco distal de la muñeca (en brazalete).

so a variar en cifras de hasta 10⁰ (7). No obstante, para fines prácticos, el ángulo atd es el más empleado.

La posición del trirradio, cualquiera que sea la forma en que se mida, tiene valor como signo físico en el diagnóstico de las anomalías cromosómicas, donde usualmente se encuentra en posición distal.

d. Surcos de flexión:

Trátase de impresiones palmares asociadas, pero distintas a los dermatoglíficos. Representan las áreas de flexión de las palmas y los dedos. Tienen una disposición constante aunque existe un cierto grado de variabilidad individual. Así podemos reconocer un surco distal en la muñeca (*surco distal de la muñeca*), el surco más distal de la palma de la mano (*surco transversal distal*, "línea del corazón"), el surco más proximal (*surco transversal proximal*, "línea de la cabeza"), y la línea larga que transcurre en la eminencia tenar, el *surco longitudinal radial* ("línea de la vida"). Podemos, además, reconocer los surcos de flexión de los dedos: las líneas metacarpofalángicas y las interfalángicas. También pueden observarse el surco del dedo medio, el surco del cuarto dedo, del quinto dedo y el surco hipotenar (figura 6).

En algunas personas, los surcos transversos distal y proximal se encuentran unidos, formando un surco único conocido como surco de simio, surco transversal simple o surco de los cuatro dedos. Este puede ser un hallazgo normal, aunque está usualmente relacionado con aberraciones cromosómicas. Un surco de simio parcial o incompleto estaría formado por dos surcos transversos entrecruzados y con una ramificación que surge de uno de ellos (figura 7). Si existe un surco de simio al cual corre paralelo otro surco transversal distal, nos encontramos ante la llamada línea de Sydney.

Recientemente, Alter (10), realizó un estudio sistemático de los surcos de flexión en 100 varones y 100 hembras normales de EE. UU., evaluando cada mano por separado. Observó que el surco tenar (surco longitudinal radial) con frecuencia es simple, y que termina en el borde radial de la palma. Un 30 por ciento de la población normal tiene un surco tenar doble en una o ambas manos. De un 5-10 por ciento tienen un surco tenar en cascada o fragmentado y en tan sólo un 0.5 por ciento lo tienen corto. El surco transversal proximal usualmente termina a nivel del cuarto dedo en el 90 por ciento de las personas, y a nivel del dedo medio o a través de la palma (surco de simio) en el resto de los casos. En el referido estudio, el surco de simio se observó solamente en el 1 por ciento de los estudiados. El surco transversal distal se encuentra en un

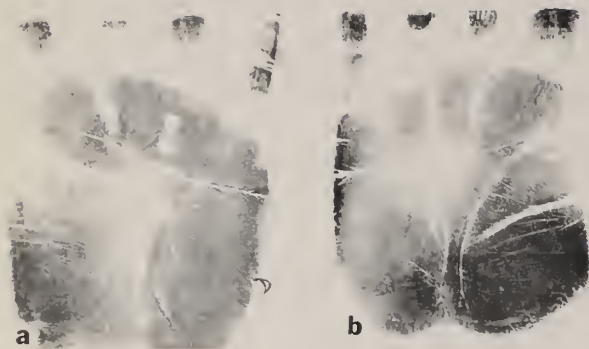


Fig. 7: Surco de simio: a) completo y b) incompleto o parcial.



Fig. 8: a) Diagrama que refleja el recuento de pliegues de un espiral bucle doble. C.D. = 10/21; b) Bucle con recuento de pliegues bajo. C.D. = 2; c) Espiral y bucle cubital en un mismo dedo. Patrón extremadamente raro. C.D. = 24/12/4.

2 por ciento de los casos y existe un surco distal accesorio en el 7 por ciento de los normales. En el 20 por ciento de la población termina entre el dedo índice y el dedo medio.

3. Impresiones de los pies:

Las impresiones dermopapilares de los pies pueden ser similares a las encontradas en los dedos y palma de la mano. A diferencia de éstos, su estudio ha sido inadecuado, limitándose, fundamentalmente, a los patrones del área halucal, donde podremos encontrar bucles distales grandes o pequeños, peroneales o tibiales, con trirradio solo o simplemente un campo abierto, además de los conocidos patrones básicos.

4. Recuento de pliegues de los dedos:

Se le llama recuento de pliegues o recuento dérmico a la suma de pliegues que cruza una línea trazada desde el punto central del trirradio hasta el centro del patrón. Inicialmente esta medida fue descrita por Galton en 1895 (11), pero las normas que actualmente se emplean fueron dictadas por Henry en 1901 (12). El pliegue o punto central del trirradio no se cuenta, co-

mo tampoco el último pliegue, si éste es el pliegue o islote central del patrón. Los pliegues que son producto de una bifurcación que se entrecruzan con la línea, se cuentan, pero no los que se encuentran cerca y no la cruzan.

En los arcos y los arcos en tienda no se cuentan surcos, su recuento dérmico es cero. En raras ocasiones los bucles pueden tener un conteo de cero. Cuando hay dos bucles o un torbellino, se pueden hacer dos conteos. Las líneas del trirradio al centro del patrón, en este caso, no deben entrecruzarse. Un torbellino concéntrico presentará el mismo conteo a ambos lados. Como existen tres trirradios habrán tres posibles conteos. Como norma, siempre se empleará para efectos de conteo y estadísticas, el recuento mayor (figura 8).

Resumen

Consideramos imprescindible para el clínico, independientemente de su especialidad, conocer los fundamentos del estudio de los dermatoglíficos y surcos de flexión, ya que empleados correctamente, son muy útiles para la orientación diagnóstica en múltiples afecciones que al analizarlas a fondo se nos presentan como condiciones hereditarias o aberraciones cromosómicas. La apatía que ha predominado hasta el momento, reside fundamentalmente en el desconocimiento de los patrones básicos y la escasa divulgación de éstos en las distintas ramas de la medicina.

En comunicaciones posteriores expondremos con detalle sus aplicaciones clínicas teniendo en cuenta las posibles variaciones que pueden existir en una población como la nuestra. Esto último constituye de por sí un estudio que se está llevando a cabo.

Summary

The study of the dermatoglyphics and flexion creases of the hands and feet has become a most useful tool for the clinician, since characteristic patterns have been found to be associated with several disease entities. Indeed, the diagnosis of Down's syndrome, for instance, is now possible without chromosomal analyses, using only dermatoglyphic findings. In this paper, the first of a series on this subject, we have introduced some of the basic concepts in the study of the dermopapillary impressions. The characteristics for the recognition of the various patterns, the loop, whorl, arch and tented arch, have been presented. The modes of measuring the atd angle have been discussed, as well as the way of performing the ridge counts. Available normal values for these

parameters have been given, although admitting that these values may differ for the population of Puerto Rico. An ongoing research project, which will be the object of another communication, will clarify this point. The dermatoglyphic findings characteristic of various pathological disorders will be presented later.

Reconocimiento

Agradecemos al Dr. Manuel E. Soto-Viera la lectura crítica del manuscrito.

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Editorial

DEXTRAN 40 -- PARADOX OF TREATMENT

Low molecular weight dextran (dextran-40) has been widely used in the treatment of poor perfusion states such as myocardial infarction, pulmonary embolism, surgical shock, cerebral ischemia, and occlusive vascular disease. It has been recommended in the prevention of acute renal failure and it seems paradoxical that the administration of dextran-40 may indeed produce acute renal failure. The first few reports of acute renal failure following dextran-40 were of great concern to Pharmacia AB and in 1967, an international conference on dextran and renal function was held in Uppsala, Sweden. At least 50 cases of acute renal failure associated with dextran-40 were reported. However, if we consider the large number of infusions of dextran-40 given throughout the world, the incidence of associated acute renal failure is low.

The interest in dextran-40 anuria or oliguria has been widespread and a dextran-40 anuria experimental model has been reproduced in various laboratories. Recently, studies performed in dogs by Chinitz, et al suggest that a decrease in perfusion pressure on the kidney in the presence of a high concentration of dextran-40 within the tubules lead to tubular plugging due to the hyperviscosity of dextran-40. In their experiments, ethacrynic acid and mannitol prevented dextran precipitation by blocking tubular reabsorption of filtrate.

In this issue of the Boletín, Burgos and Figueroa report a patient with acute oliguric renal failure that, after the administration of dextran-40, was successfully treated with periodic hemodialysis until recovery. In contrast to other reported cases in man, absolute clinical evidence for a precipitating factor was lacking. However, surgery, anesthesia, and trauma may alter renal perfusion pressure and tubular water reabsorption enhancing the intratubular precipitation of dextran-40, similar to the dog experiments. Nevertheless, the precise mechanism producing renal failure in this patient is not altogether clear. At this time, studies are necessary to gain further insight into the pathogenesis of dextran-40 anuria.

In the meantime, it is extremely important for the clinician to recognize that dextran-40 can produce renal failure. Urine flow rates must be carefully monitored by the use of an indwelling Foley catheter whenever dextran-40 is administered. If oliguria is present at any time, the infusion of dextran-40 is discontinued and a potent diuretic such as mannitol, ethacrynic acid or furosemide is indicated.

José L. Cangiano, MD

Reference

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Pathophysiology and Prevention of Dextran-40 Induced Anuria, J. Lab. Clin. Med. 77: 76, 1971.

NOTICIAS

From the American Diabetes Association:

The Nineteenth Postgraduate Course, Diabetes in Review: Clinical Conference, 1972, will be held at the Sheraton-Four Ambassadors Hotel, Miami, Florida, on January 24, 25 and 26, in cooperation with the University of Miami School of Medicine. The Postgraduate Courses are presented annually by the Committee on Professional Education of the American Diabetes Association, chaired by Karl E. Sussman, M. D., of Denver.

The American College of Physicians presents Diagnosis and Management of Infectious Diseases, February 23-25, 1972, University of California School of Medicine.

This course will present recent advances in diagnosis and therapy and will consider infectious disease problems which are especially perplexing for the clinician. Several new compounds have appeared or are imminent which have activity against various classes of infectious agents and innovations in therapy will be considered comprehensively. Although practical aspects will receive emphasis, basic mechanisms of disease and clinical pharmacology will be included. The increasing importance of infection in patients with impaired host resistance is recognized and the approach to diagnosis and management of these different problems will receive attention. Audience participation in the discussion and question periods will be expected.

Please send all registration, requests for information, and application to: Registrar, Postgraduate Courses, American College of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania, 19104.

The American College of Physicians presents The Physiological Basis of Clinical Disease - March 6-9, 1972, University of Texas Southwestern Medical School, Dallas, Texas.

This course is designed to provide an understanding of the basic physiologic concepts of disease and the practical application of these concepts to the understanding of clinical disorders of man. The pathophysiology of such diseases as hypertension, diabetes mellitus, pulmonary disorders, cardiovascular disease, and the disorders of the immunologic system, as well as liver diseases and gastroenterologic derangements will be examined in detail. In each case the underlying physiologic derangements will be employed as the basis for providing a rational means of diagnosing and treating the disease in question.

Please send all registrations, requests for information, and application to: Registrar, Postgraduate Courses, American College

of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania, 19104.

The American College of Physicians presents Advances in Clinical Endocrinology - March 7-10, 1972, Boston University Medical Center, Boston, Massachusetts.

This course is intended to summarize recent progress in endocrinology as applied to the diagnosis and therapy of specific endocrine disorders. The program will be comprehensive in providing up-to-date information on the physiological basis of the newer clinical diagnostic tests of endocrine function. Similarly, current therapeutic management and its rationale will be provided for the various hormonal disorders. Lectures, panels and case presentations will be used to enhance the understanding of the major endocrine disorders. The faculty will consist of eminent physicians from medical schools and hospitals in Boston along with guests from institutions throughout the country.

Please send all registration, requests for information, and application to: Registrar, Postgraduate Courses, American College of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania, 19104.

From the American Academy of Pediatrics News Release:

EVANSTON, Ill. — The procedure of abortion for teen-age girls must never become a routine technical event in the lives of young people, the American Academy of Pediatrics has cautioned in a statement appearing in the AAP's current Newsletter.

The statement, prepared by the Academy's Committee on Youth, and endorsed by its Council on Child Health, emphasizes that "every effort must be made to insure that a concerned, dignified, and enlightened care situation is developed for these young patients."

Stressing that the American Academy of Pediatrics prefers neither to sanction nor to forbid the use of abortion to terminate an unwanted pregnancy in the teen-age girl, the AAP states that it "does have the responsibility to insist that physicians considering this recourse provide for appropriate counseling and support for those adolescent girls and other involved persons, including the young fathers."

Also important is the need for the pediatrician who is unable to adequately provide counseling support to act as the pivotal person in arranging for a social worker, pastor, or other experienced counselor to provide this essential care, both before and after the procedure.

Continuing, the Academy points out that the pediatrician must make certain that adequate information and sex counseling are available to his teen-age patients. The AAP further urges in its statement that contraceptive advice and prescription for the sexually active teen-age girl should be accompanied by investigation and alteration of contributing issues wherever possible.

"Continuing long-term support directed toward facilitating personality development is an integral part of the care situation. Abortion must never be allowed to replace adequate preventive care or contraceptive measures."

Indicating that although abortion is a possible solution to an unwanted pregnancy in a teen-age girl, the Academy emphasizes that this procedure itself is often replete with problems, ambivalent feelings, and guilt.

"The pregnant teen-ager is often alone, or feels alone, is frightened, frequently estranged from her family and, on occasion, emotionally disturbed. The physician, using tactful persuasion and appeal, should make every attempt to have the girl involve her parents in making her decisions. Handled with care and concern, it is possible at times for reconciliation in family relations to take place, bringing parents and daughter into a mutually supporting role."

The statement also points out that the physician entrusted with the care of an adolescent girl frequently must serve as her advocate.

"He should try to help her make an appropriate decision regarding her pregnancy," the statement urges. "If she elects abortion, the physician must determine that the procedure will be conducted under optimum medical conditions by a skilled accredited physician."

"The physician advocate must safeguard the physical and emotional welfare of the essentially defenseless teen-age patient and in so doing protect her rights of confidentiality," the statement affirms.

The Academy concludes by emphasizing that the decision by the patient to terminate her pregnancy by abortion does not end her need for further care.

"Continuing support and guidance are the essentials of a rehabilitative program with the pediatrician acting as the coordinator. In addition, encouragement of continued education, job training, and assistance with employment must follow."

From the American Medical News - Dec. 21, 1970:

MD'S SUE FOR MEDICAID FEES - Physicians in Massachusetts have gone into court to force the state Rate Setting Commission to consider new Medicaid rates.

Louis F. Alfano, MD, chairman of the Massachusetts Me-

dical Society's Subcommittee on Tax-Supported Medical Care, and Thomas A. Flaherty, MD, a committee member, filed a petition in Superior Court in Suffolk County as a class action on behalf of all physicians in the state providing services under Medicaid.

The physicians acted after the Rate Setting Commission denied a petition to review the rates for physician, laboratory, and x-ray services.

ACCORDING TO the Massachusetts Medical Society, physicians' services to Medicaid patients are now being reimbursed on the basis of a fee schedule originally devised in 1950, and modified in 1957. The fees do not even reflect cost of living increases over a period of many years, the society said.

From the FDA Drug Bulletin - December 1971:

HEXACHLOROPHENE AND NEWBORNS - A number of recent studies have raised serious questions concerning the toxicity of hexachlorophene preparations used for total body bathing of newborn infants. A summary of three such studies follows:

1. Fifty newborn infants, bathed daily with a 3 percent hexachlorophene product, showed hexachlorophene blood levels of .009 to .646 micrograms/ml. on the day of hospital discharge. No obvious toxic symptoms were noted in the newborns. (Curley, A., et al. *Lancet*, Aug. 7, 1971.)

2. Rats fed hexachlorophene to achieve mean hexachlorophene blood levels of 1.21 micrograms/ml. showed brain changes characterized by cerebral edema limited to the white matter, and cystic spaces of the brain believed produced by fluid accumulation. (Gaines, T. B., Kimbrough, R. D. Paper read at the 10th annual meeting of the Society of Toxicology, Washington, D. C., March 7-11, 1971. See also Kimbrough & Gaines, *Arch. Environ. Health* 23: 114-118, Aug. 1971.)

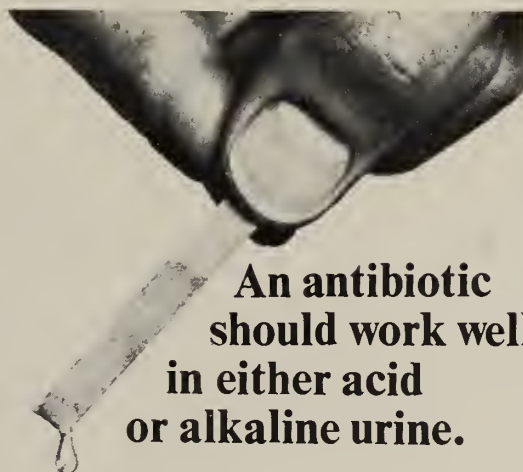
3. Newborn monkeys washed daily with 3 percent hexachlorophene for 90 days showed mean hexachlorophene plasma levels of 2.3 micrograms/ml. When they were sacrificed, the white matter of the brain, particularly the cerebellum, brain stem and all parts of the cord, showed lesions consisting of cystic spaces like those described above. (Studies submitted by Winthrop Laboratories to FDA on November 18, 1971.)

These studies challenge the safety of hexachlorophene bathing of infants, a practice which has been widely advocated as effective prophylaxis against nursery epidemics of staphylococcal skin infections. A critical review of the studies on which this claim is based indicates that whereas there is no doubt that hexachlorophene bathing decreases skin colonization of gram-positive organisms, there is a lack of substantial evidence that hexachlorophene washings by themselves prevent staphylococcal disease or show antibacterial activity against gram-negative organisms. Hospitals are known to operate nurseries safely without the use of this product.

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Warning: In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

Precautions: Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects: Gastrointestinal system — anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin — maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney — rise in BUN, apparently dose-related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth — dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy. Demethylchlortetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.

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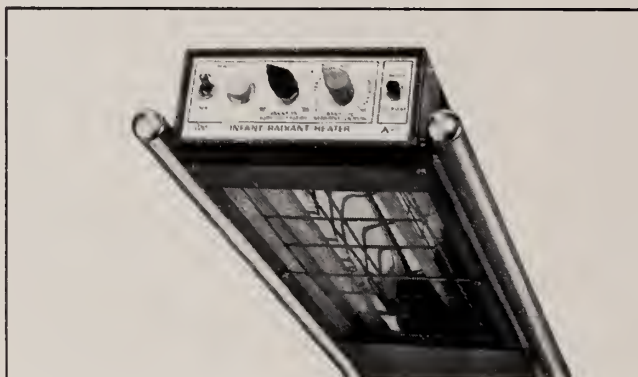
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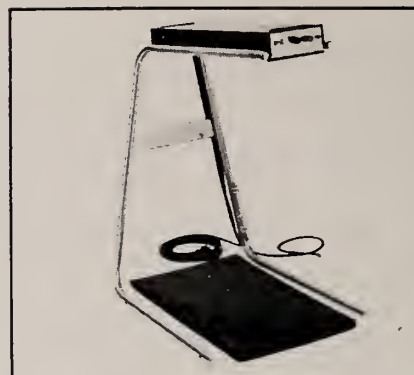
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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures.

Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision.

Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose™ packages of 1000.



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EDICION DE LA SECCION DE CARDIOLOGIA PEDIATRICA
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TETRALOGIA DE FALLOT: CONCEPTOS ACTUALES DE SU TRATAMIENTO 17

Rafael Villavicencio, MD, Jorge Sánchez, MD y Amalia Martínez Picó, MD

CONSTRICCION QUIRURGICA DE LA ARTERIA PULMONAR: 23

Experiencia en 80 Casos

Agustín Muñoz, MD, Edda Torres de Arraut, MD y Amalia Martínez Picó, MD

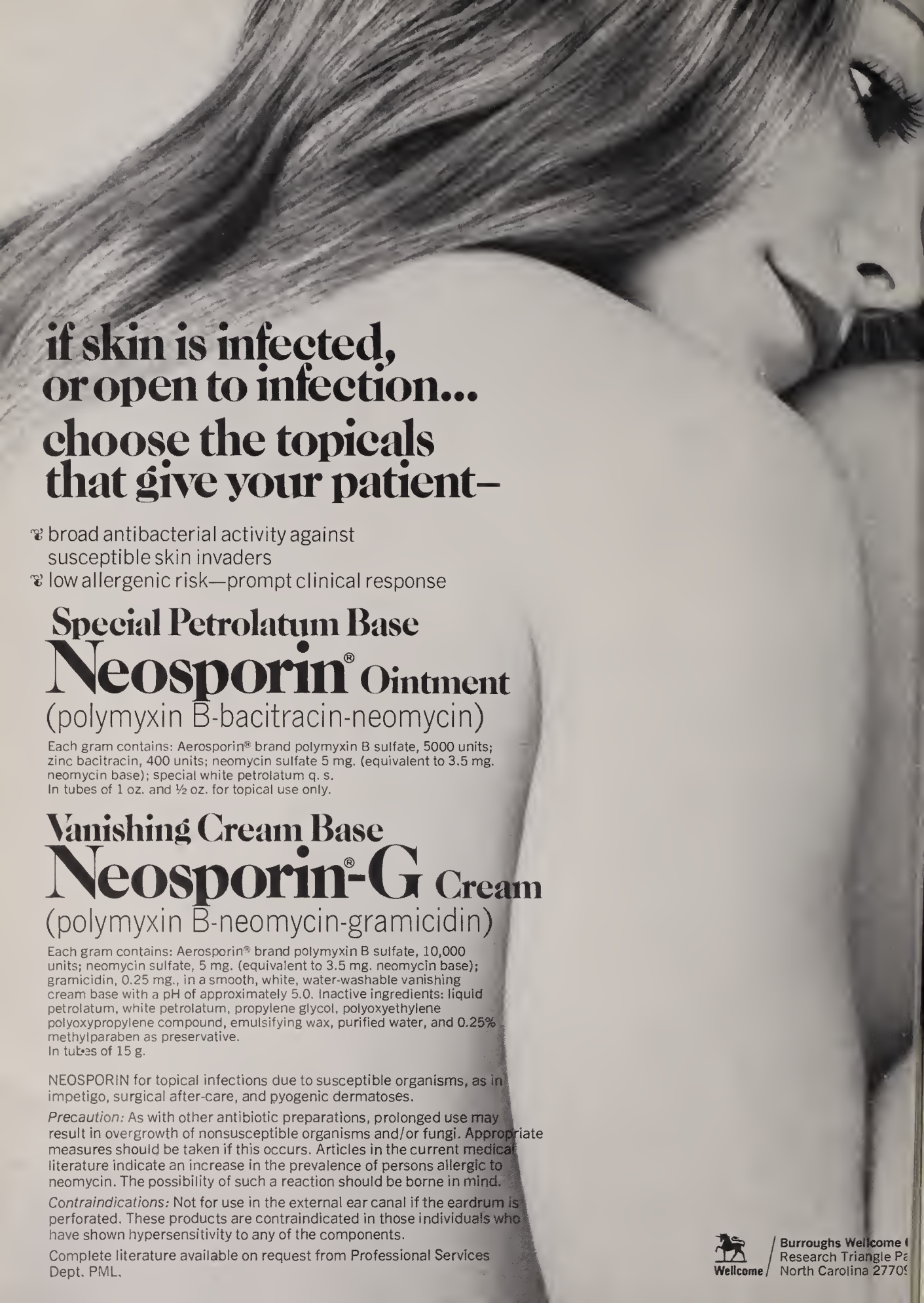
MARCAPASOS EN NIÑOS: *Diez Años de Experiencia Clínica* 31

Mercedes Vega Vidal, MD

EDITORIALES 39

Cardiología Pediátrica: Alcances en Puerto Rico
Ejemplo, Problemas y Preguntas

NOTICIAS 41



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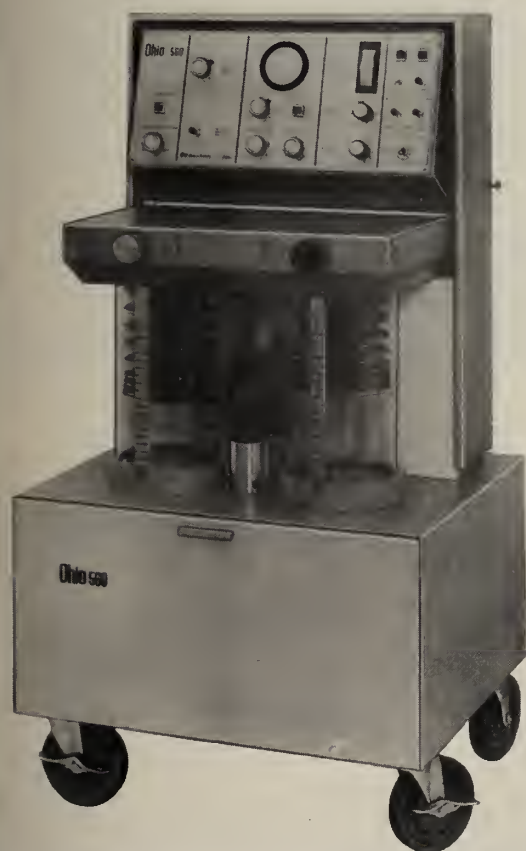
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Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; dermatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, presence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially to obtain predictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

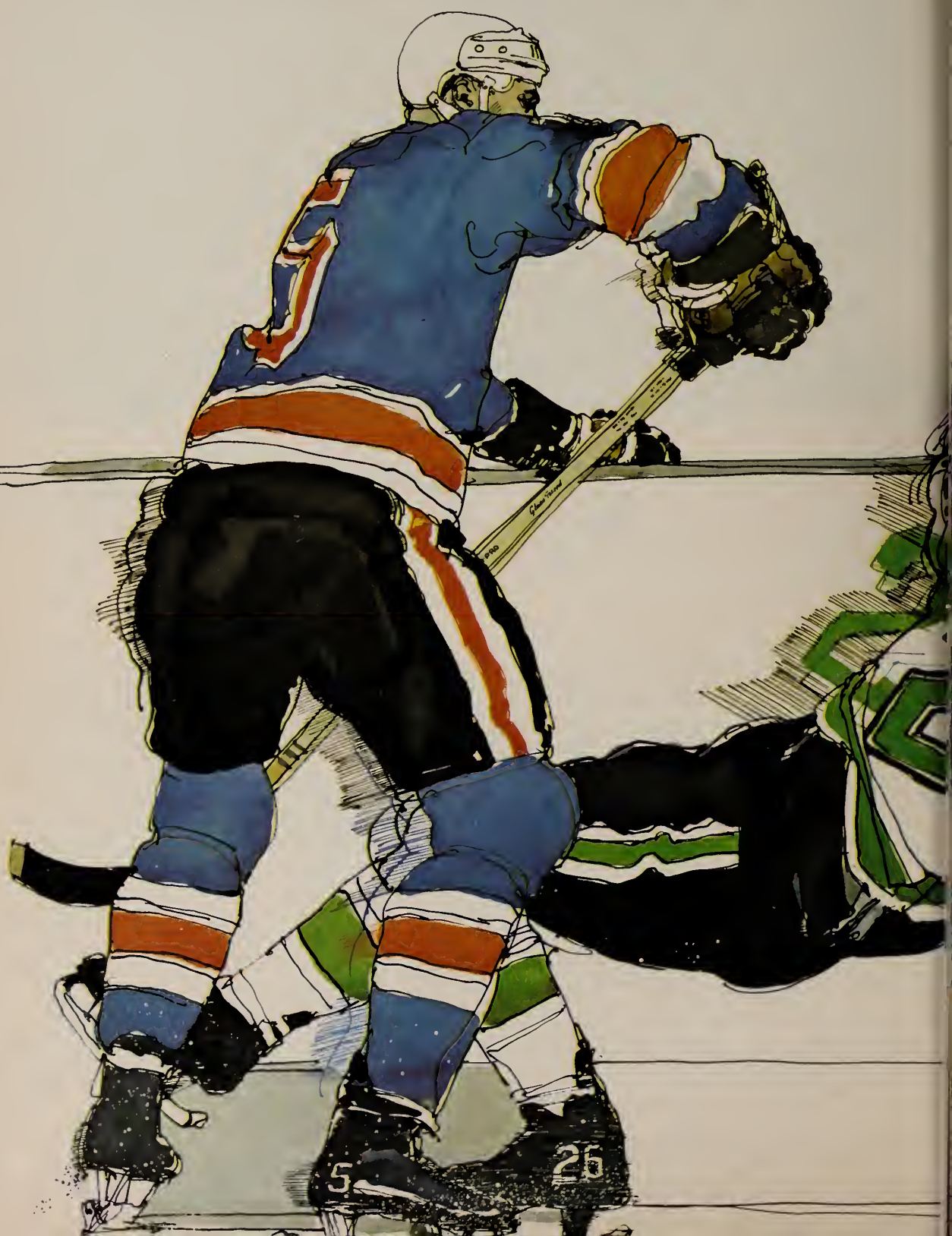
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-800-E

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For the skeletal muscle spasm of back sprains, Valium® (diazepam) can be a valuable adjunct. A dose of 2-10 mg, three or four times a day, goes to work to help break up the cycle of spasm/pain/



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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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- | | |
|--|--|
| ¿Le molestan coyunturas o músculos rígidos o dolorosos? | 1. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Se le hinchon las coyunturas? | 2. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Le molestan dolores en la espalda u hombros? | 3. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Le duelen los pies con frecuencia? | 4. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Está deshabilitado en alguna manera? | 5. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Tiene algún problema con su piel? | 6. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Le pica o quema la piel? | 7. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Sangra por largo tiempo cuando se hace una pequeña cortadura? | 8. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Se lastima fácilmente formando un cardenal o morete? | 9. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Se ha desmayado o se ha sentido como que se va a desmayar? | 10. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Tiene alguna parte del cuerpo siempre adormecida? | 11. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Ha tenido alguna vez convulsiones? | 12. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Le ha cambiado ultimamente su letra al escribir? | 13. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Tiene tendencia a temblar o menearse mucho? | 14. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Se pone nervioso en presencia de personas extrañas? | 15. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Se le hace difícil tomar decisiones? | 16. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Se le hace difícil concentrar o recordar? | 17. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Se siente solo o deprimido? | 18. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Llora a menudo? | 19. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Diría usted que tiene una perspectiva irremediable? | 20. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Tiene dificultad en relajar o reposar? | 21. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Tiene a preocuparse demasiado? | 22. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Le molestan o asustan algunos sueños o pensamientos? | 23. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Tiene a ser tímido o sensitivo? | 24. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Se molesta mucho cuando lo critican? | 25. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Pierde el genio con frecuencia? | 26. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Cosas pequeñas lo hacen molestar? | 27. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| ¿Le molesta cualquier trabajo o problemas familiares? | 28. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Tiene algún problema con su vida sexual? | 29. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Ha considerado alguna vez suicidarse? | 30. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| ¿Ha deseado alguna vez, o buscado, ayuda psiquiátrica? | 31. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |

13. MUSCULOSKELETAL

- ☒ aching muscles or joints
- ☐ swollen joints
- ☒ back or shoulder pains
- ☐ painful feet
- ☐ handicapped

14. SKIN

- ☐ skin problems
- ☐ itching or burning skin
- ☐ bleeds easily
- ☐ bruises easily

15. NEUROLOGICAL

- ☐ faintness
- ☒ numbness
- ☐ convulsions
- ☐ change in handwriting
- ☐ trembles

16. MOOD

- ☒ nervous with strangers
- ☒ difficulty making decisions
- ☒ lack of concentration or memory
- ☐ lonely or depressed
- ☐ cries often
- ☐ hopeless outlook
- ☒ difficulty relaxing
- ☒ worries a lot
- ☐ frightening dreams or thoughts
- ☐ shy or sensitive
- ☒ dislikes criticism
- ☒ loses temper
- ☒ annoyed by little things
- ☐ work or family problems
- ☐ sexual difficulties
- ☐ considered suicide
- ☒ desired psychiatric help

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When your patient speaks little English and your Spanish is limited or nonexistent, you need the new ROCOM Health History Questionnaire (Spanish).*

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We're not against all her E.coli...

only the E.coli in her
urinary tract

Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis*...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. And it does not suppress normal bac-

**Basic in cystitis*, pyelitis*,
pyelonephritis***

The one-tract action of *Macrochantin*® Capsules
(nitrofurantoin macrocrystals) 50mg/100mg.

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterra-

nean and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms.



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TETRALOGÍA DE FALLOT: CONCEPTOS ACTUALES DE SU TRATAMIENTO

Rafael Villavicencio, MD
Jorge Sánchez, MD
Amalia Martínez Picó, MD

La Tetralogía de Fallot es la cardiopatía cianótica congénita más frecuente. Constituye el 11 por ciento de todos los pacientes con cardiopatía congénita en las series de Keith (1) y el 30 por ciento de las cianóticas. Solamente la sobrepasan el defecto interventricular (25 por ciento) y el conducto arterioso patente (12 por ciento).

La cirugía cardíaca permite la cura total de estos pacientes, el rol importante del pediatra es protegerlos hasta la edad aconsejable para cirugía correctiva.

El paciente con Tetralogía tiene cianosis de intensidad variable, generalmente se pone en cuclillas y puede o no tener episodios anóxicos. Presenta un soplo de estenosis pulmonar, con un componente pulmonar del segundo sonido disminuido o ausente, un corazón pequeño en forma de bota con vascularidad pulmonar disminuida en la radiografía de tórax (Fig. 1) e hipertrofia ventricular derecha en el electrocardiograma (Fig. 2).

El propósito de este artículo es el de revisar y exponer los medios disponibles para el tratamiento médico y quirúrgico de la Tetralogía de Fallot, tanto el paliativo como el curativo.

Episodios Anóxicos

Los niños con tetralogía tienen problemas de alimentación y retardo en su crecimiento. Ocurren también complicaciones sumamente peligrosas como son los episodios anóxicos y los fenómenos tromboembólicos, que pueden causar la muerte del paciente o afectar severamente su desarrollo mental. Estos episodios se conocen también por ataques anóxicos, ataques sincopales, disnea paroxística o hiperepnea paroxística; todos describen como el paciente se torna irritable, taquipneico y más cianótico, estado que al progresar llega a la flacidez generalizada, pérdida del conocimiento y la muerte en un intervalo variable desde varios minutos

hasta varias horas. La pérdida del conocimiento se debe a una hipoxia cerebral acompañada cuando es severa, de bradicardia, la cual es un signo de suma gravedad (2).

La mayor incidencia de estos episodios ocurre entre los dos y tres meses de edad, pero pueden aparecer desde el nacimiento hasta los tres o cuatro años. Tienden a presentarse mayormente en la mañana al despertar el



Fig. 1: Radiografía de tórax característica de la Tetralogía de Fallot. Nótese la marcada disminución de la vascularidad pulmonar, el corazón pequeño con el ápice hacia arriba y la concavidad en el área de la pulmonar.

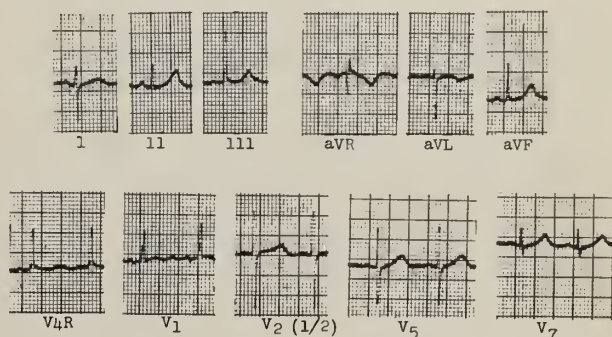


Fig. 2: Electrocardiograma de paciente con Tetralogía de Fallot. Se demuestra hipertrofia ventricular derecha con patrón de sobrecarga sistólica y una desviación del eje eléctrico hacia la derecha.

paciente (3), y aunque a veces no existen causas precipitantes en muchas ocasiones pueden ser desencadenadas por factores fisiológicos como el llorar, comer o defecar. Factores patológicos como la fiebre, la acidosis, la tos, la deshidratación y la taquicardia supraventricular (4), también pueden ocasionarlos. Ciertas drogas como el Iso-proterenol (Isuprel*), que estimulan los receptores adrenérgicos beta y disminuyen la resistencia periférica producen un episodio anóxico típico (5).

Estos pacientes pueden tener un pH y pCO_2 normales durante el sueño con el pO_2 ligeramente disminuido y se encuentran generalmente en un balance metabólico.

Existen varias explicaciones para los procesos anóxicos. La contracción muscular del infundíbulo del ventrículo derecho no puede explicar los episodios anóxicos que se producen en la atresia pulmonar. La teoría de Guntheroth (3) parece más aceptable: la hiperpnea en un niño normal aumenta el pO_2 y el pH, y disminuye el pCO_2 . En el paciente con tetralogía la hiperpnea aumenta el flujo sistémico debido a una disminución de la resistencia periférica, esto a su vez aumenta el cortocircuito de derecha a izquierda en vista de que el flujo pulmonar no aumenta concomitantemente al flujo sistémico. Este aumento del cortocircuito disminuye el pO_2 y el pH y aumenta pCO_2 . Cuanto más hiperventilación hay, más hipóxico y acidótico se pone el paciente creándose así un círculo vicioso que tiende a persistir (Diagrama I).

Los episodios anóxicos constituyen una verdadera emergencia y requieren un tratamiento enérgico e inmediato:

1. *Posición* – El paciente debe colocarse con las piernas flexionadas sobre el tórax si es infante, o en cuclillas

si es mayorcito. Ambas posiciones atrapan la sangre venosa en las piernas que tiene una saturación muy baja de oxígeno, de manera que la sangre que llega al corazón derecho es de la circulación visceral y está mejor saturada. Se disminuye el cortocircuito de derecha a izquierda por encontrarse la resistencia periférica aumentada y se corta así el estímulo para la hiperpnea e hiperventilación.

2. *Oxígeno* – Está indicada la administración de oxígeno en una concentración al 100 por ciento, aunque sus beneficios son limitados debido a que el retorno venoso pulmonar de sangre oxigenada es pequeño.

3. *Morfina* – Su eficacia ha sido probada desde hace 23 años por Taussig (6). Se la administra en una dosis de 1 mg. por cada 10 libras de peso por vía intramuscular. La morfina deprime el centro respiratorio y disminuye la hiperventilación y también secuestra la sangre venosa en las extremidades (7).

4. *Bicarbonato de Sodio* – Si durante el episodio anóxico disminuye la saturación de oxígeno arterial un 40 por ciento o menos, aumenta el metabolismo anaeróbico con acumulación de lactato y producción de acidosis. La administración de bicarbonato por vía endovenosa corrige esta acidosis metabólica y puede así interrumpir el episodio anóxico como lo ha demostrado Rudolph (8). En dosis adecuadas el bicarbonato actúa restableciendo el pH a niveles normales aunque el aumento que produce el pO_2 es discreto. La dosis recomendada es de 1 mEq. por kilo por cada unidad de 0.1 de pH por debajo de 7.35. Cuando no se sabe el pH se puede asumir uno de 7.2 y administrar 1 mEq. por kilo lentamente por vía endovenosa.

5. *Propranolol* – (Inderal*) es un agente que bloquea los receptores adrenérgicos beta del miocardio; existe amplia evidencia de que este agente es efectivo en la terminación y también en la prevención de los episodios anóxicos (2, 5, 9, 10). El bloqueo de los receptores beta disminuye el cortocircuito de derecha a izquierda, reduce el gradiente de presión entre el ventrículo derecho y la arteria pulmonar, aumenta el calibre del tracto de salida del ventrículo derecho y por lo tanto aumenta el flujo pulmonar. La dosis que se recomienda es de 1 mg. por cada 10 libras de peso, lentamente por vía endovenosa. En el Hospital Universitario diluimos esta cantidad en 50 cc. de solución intravenosa y la administramos en 10 minutos, observando cuidadosamente la presión arterial y el pulso del paciente ya que el Propranolol disminuye ambos.

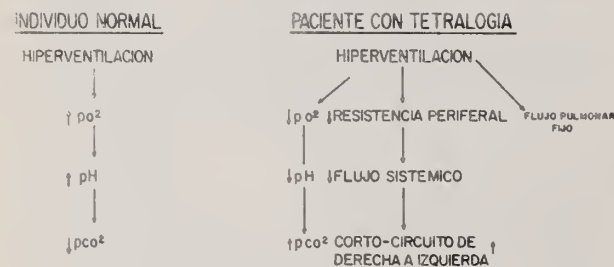


Diagrama I: Representación esquemática del mecanismo de los episodios anóxicos en los pacientes con Tetralogía de Fallot de acuerdo con la teoría expuesta por Guntheroth.

* - Nombre comercial.

* - Nombre Comercial. Ayerst Lab.

En muchos pacientes el Propranolol evita las recurrencias de estos episodios, especialmente aquellos en los que el tracto de salida del ventrículo derecho se abre bastante durante la sístole.

Además de prevenir las recurrencias también contribuye al bienestar del paciente y mejora la tolerancia de ejercicio, pues se ha comprobado en el laboratorio por uno de los autores (J. S.) que cuando a un paciente con tetralogía se le administra Propranolol y se le somete a una prueba controlada de ejercicio, como es el ergómetro de bicicleta, este tolera más carga por más tiempo y su saturación de oxígeno no cae tanto como cuando se le somete a la misma clase de ejercicio sin haberle administrado Propranolol. Además la recuperación y la deuda de oxígeno son menores.

La dosis oral aconsejada es de 20 a 60 mgrs. (5, 10) al día, divididas en varias dosis de acuerdo a las necesidades. El Propranolol no reemplaza a la cirugía paliativa y todo niño que tiene episodios anóxicos necesita ser operado. Esta droga simplemente prolonga el período de espera para la cirugía.

6. *Medidas Generales* — Tienden a prevenir los episodios anóxicos y comprenden desde la supresión de factores precipitantes como el uso de laxantes en niños estreñidos o la sedación ligera de pacientes irritables hasta la corrección rápida de la deshidratación, pues se sabe que el volumen plasmático se halla disminuido debido a la policitemia compensadora. También la anemia de estos pacientes requiere atención especial. Se puede asumir que una hemoglobina menor de 15 gms. en un paciente cianótico indica la necesidad de terapia con hierro, a veces con resultados dramáticos (11).

Fenómenos Tromboembólicos e Infecciones

Debemos considerar ante todo los abscesos cerebrales, que son más frecuentes después de los dos años de edad. De los ocho pacientes cianóticos con abscesos cerebrales en el Hospital for Sick Children de Toronto (12) durante un período de 10 años, 4 tenían Tetralogía de Fallot. Casi nunca se aísla un microorganismo específico. Más bien que deberse a embolos sépticos se cree que un pequeño infarto cerebral puede infectarse por una de las transitorias y frecuentes bacteremias. La mortalidad de 50 por ciento asociada a esta complicación exige que el médico esté muy alerta para detectar un absceso que puede manifestarse como un simple dolor de cabeza o ligera hipertermia.

Las trombosis cerebrales guardan estrecha relación con la hiperviscosidad sanguínea, especialmente cuando el hematocrito excede del 65 por ciento. La hipoxia

juega un rol importante también. No deberá permitirse que estos pacientes alcancen unos hematocritos del 70 por ciento y aunque la plasmaféresis (13) puede ayudarlos temporalmente, lo que ellos necesitan de urgencia es la cirugía.

Tratamiento Quirúrgico

Comprende la corrección total y las operaciones paliativas. Después de la primera el paciente queda anatómica y fisiológicamente curado, a no ser que ocurran complicaciones.

Cirugía Paliativa

Generalmente se lleva a cabo en los pacientes sintomáticos que son demasiado pequeños para corrección total. Esta última requiere circulación extracorpórea que a edad temprana conlleva una mortalidad y morbilidad elevadas. Con cirugía paliativa adecuada desaparecen los episodios anóxicos, el paciente tolera mejor el ejercicio y hasta se producen cambios favorables en la personalidad. Aunque la baja del hematocrito disminuye la frecuencia de los fenómenos tromboembólicos, el peligro de la endocarditis y el de los abscesos cerebrales continúa igual. Una desventaja de los cortocircuitos aortopulmonares quirúrgicos es la hipertensión pulmonar tardía por el excesivo flujo sanguíneo a los pulmones.

El objeto de todos los procedimientos paliativos es aumentar la cantidad de sangre que llega a los pulmones por medio de una anastomosis de una arteria sistémica a una de las ramas pulmonares. Son tres los procedimientos usados con más frecuencia.

1. *Anastomosis de la arteria subclavia con una rama pulmonar (Blalock-Taussig).*

Es la operación paliativa de elección, tiene la ventaja de que nunca lleva a fallo cardíaco debido a que el cortocircuito está limitado por el tamaño de la arteria subclavia y además no ocasiona dificultades técnicas durante la corrección total. Consiste en anastomosar la subclavia del lado opuesto al arco de la aorta con la arteria pulmonar correspondiente (Fig. 3).

Su principal desventaja consiste en el lumen de la anastomosis, a veces resulta ser muy pequeño y por lo tanto insuficiente, o se ocluye con facilidad. Nosotros la usamos en pacientes mayores de dos años de edad.

En los últimos cinco años en el Hospital Universitario se han llevado a cabo 14 anastomosis de este tipo, la edad de los pacientes fluctúa entre los 6 meses y los 5

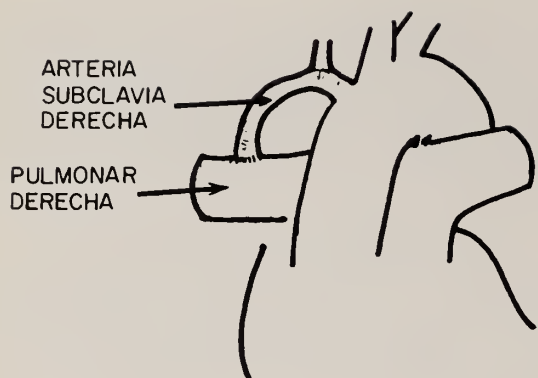


Fig. 3: Ilustra la anastomosis termino-lateral de la arteria subclavia con la pulmonar del mismo lado. (Tipo Blalock-Taussig.)



Fig. 4: Anastomosis latero-lateral entre la aorta descendente y la arteria pulmonar izquierda (Operación de Potts).

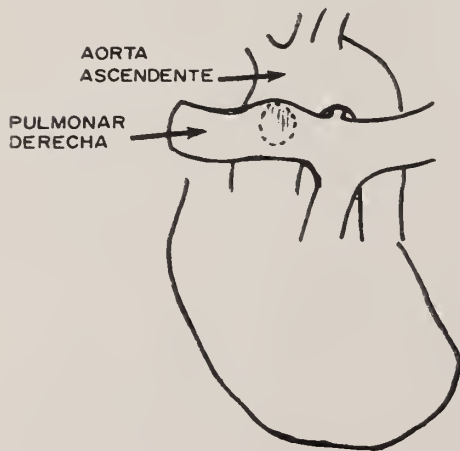


Fig. 5: Anastomosis latero-lateral entre la aorta ascendente y la arteria pulmonar derecha (Operación de Waterston).

años. Ocurrieron dos muertes relacionadas con el procedimiento para una mortalidad del 15 por ciento. De los sobrevivientes, 4 (o sea el 27 por ciento) nunca funcionaron o se ocluyeron. Esto fue comprobado por cirugía ulterior en 2, por medio de estudio radioactivo pulmonar en 1, y por autopsia en el otro. El mayor de estos cuatro pacientes tenía 15 meses de edad.

2. Anastomosis de la aorta descendente con la pulmonar (Operación de Potts).

Fácil técnicamente, con una anastomosis adecuada tiene dos grandes desventajas:

1. Es muy difícil de reparar durante la cirugía correctiva.

2. La anastomosis es grande y con el tiempo aparece en algunos casos insuficiencia cardíaca o hipertensión pulmonar irreversible.

En nuestra institución se han hecho solamente tres anastomosis de Potts en un período de cinco años. La edad de los pacientes variaba entre los 10 días hasta los 7 años con ninguna mortalidad. La mortalidad de otros centros está alrededor de 9 por ciento (14).

La operación consiste en anastomosar la aorta descendente con la arteria pulmonar izquierda (Fig. 4).

3. Anastomosis de la aorta ascendente con la pulmonar derecha (Operación de Waterston) (Fig. 5).

Este es un procedimiento sencillo y puede usarse indistintamente en pacientes con arco aórtico derecho o izquierdo. Tiene una mortalidad baja y puede cerrarse fácilmente en el momento de la reparación completa. Tiene la desventaja de que es muy difícil regular el tamaño de la anastomosis. Algunos autores han sugerido que el tamaño de la anastomosis no debe pasar de 3 mm. en los pacientes de 2 años y de 4 mm. en los mayores de esta edad (15).

En nuestro hospital este ha sido el procedimiento paliativo de elección en los últimos años. Desde el año 1966 se han realizado 25 anastomosis de Waterston, de los cuales murieron 7 pacientes, todos ellos en las primeras 24 horas del postoperatorio para una mortalidad de 24 por ciento. Las edades fluctuaron entre una semana y los nueve años. La mortalidad en otros centros (15, 16, 17) de los Estados Unidos (Tabla I) es menor a la nuestra debido a que la mayoría de nuestros pacientes son referidos en una etapa muy tardía. No hemos realizado ningún otro procedimiento paliativo en nuestras tetralogías. La anastomosis de Glenn o sea la anastomosis de la vena cava superior con la arteria pulmonar derecha podría considerarse en casos mayores de 6 meses en lo que no pudieran realizarse los procedimientos anteriormente descritos.

TABLA I: OPERACION DE WATERSTON EN TETRALOGIA

Autor	No. de Pacientes	Edad	Mortalidad
Sommerville (15) (Londres)	20	11 meses - 14 años	0.0 por ciento
Waldhausen (16) (Filadelfia)	17	< 1 año - 9 años	5.8 por ciento
Bernhard (17) (Boston)	47	< 1 año	21.0 por ciento

Corrección Total

La corrección total es aconsejable en todo paciente mayor de 3 años sintomático con un peso de por lo menos 35 libras. También se hace la reparación completa en todo paciente de 4 o 5 años de edad (edad preescolar) aunque esté asintomático y es probable que en el futuro se recomiende la reparación total en la infancia.

La operación consiste en abrir el ventrículo derecho, cerrar el defecto interventricular con un parche y resear el infundíbulo para aliviar la estenosis pulmonar. En algunos casos esto es posible solo por medio de otro parche sobre el área del infundíbulo y que llegue hasta la arteria pulmonar.

Cuando la reparación total es exitosa, el paciente queda curado completamente: la cianosis desaparece y mejora la tolerancia al ejercicio. Se pueden oír soplos postoperatorios generalmente debido a una estenosis pulmonar residual que luego desaparece. Cuando se usa un parche para reparar el tracto de salida del ventrículo derecho se puede oír un soplo de insuficiencia de la válvula pulmonar, lo cual tiene pocos efectos adversos para el paciente (18, 19).

En la radiografía de tórax puede aparecer un ligero aumento de la silueta cardíaca con circulación pulmonar normal. El electrocardiograma registra la disminución progresiva de la hipertrofia ventricular derecha. La manera ideal de probar los resultados de la cirugía es la de volver a cateterizar a estos pacientes, pero en nuestro medio por razones diversas se hace solo excepcionalmente.

Se han realizado 10 reparaciones completas en nuestro hospital con una mortalidad del 33 por ciento desde enero de 1966 a junio de 1971. Otros grupos tienen una mortalidad de 8 y 13 por ciento en pacientes menores de 5 años (20, 21, 22). La mortalidad está íntimamente relacionada con la edad del paciente, la severidad de la cardiopatía y la experiencia del centro cardiovascular donde se realiza la cirugía. También influyen en la

baja de la mortalidad el buen manejo médico del paciente, el referimiento temprano y el diagnóstico hemodinámico completo y exacto.

Es nuestro empeño que en el futuro todos los pacientes con Tetralogía de Fallot lleguen a la cirugía en condiciones óptimas para que la mortalidad quirúrgica sea menor, y que los operados queden completamente rehabilitados.

Resumen

El artículo actualiza el tratamiento médico de la Tetralogía, haciendo énfasis en los episodios anóxicos y fenómenos tromboembólicos. También se revisan las diferentes técnicas quirúrgicas paliativas y correctivas. Se hace mención a los pacientes que se beneficiaron con estas operaciones en el Hospital Universitario durante un período de 5 años. Se hace énfasis en el rol del cardiólogo de mantener a estos pacientes en condiciones óptimas para la cirugía correctiva después de la cual puede el paciente quedar completamente rehabilitado.

Summary

This paper reviews the current concepts of the medical management of Tetralogy of Fallot. The anoxic spells and thromboembolic phenomena are emphasized.

The surgical techniques, both palliative and corrective are also reviewed. Particular mention is made of the patients that underwent these procedures at the University Hospital during a 5-year period.

Emphasis is made in the cardiologist's role in maintaining these patients in optimal conditions for corrective surgery so that the chances for a complete rehabilitation after surgery could be enhanced.

Reconocimiento

Queremos reiterar nuestro agradecimiento a la señora Norma C. González, a la señorita Rebeca Puente y a la señora Clara N. de Aparicio, por su valiosa asistencia en la elaboración de estos artículos.

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CONSTRICCION QUIRURGICA DE LA ARTERIA PULMONAR: *Experiencia en 80 Casos*

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Amalia Martínez Picó, MD

Desde que Muller y Damman (1) describieron la constricción quirúrgica de la arteria pulmonar hace casi dos décadas, esta operación ha sido usada extensamente como procedimiento paliativo en pacientes de cardiopatía congénita, con flujo pulmonar muy aumentado. Los resultados han sido alentadores en pacientes con fallo congestivo, que no han respondido a tratamiento médico.

Han aparecido muchos informes en la literatura médica demostrando los resultados a corto y largo plazo (2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12). Creemos que en el futuro se irá reduciendo la frecuencia con que se realice esta operación, en vista de que la edad adecuada para la cirugía correctiva será menor (13). El propósito de este artículo es el de revisar los resultados que hemos obtenido con el procedimiento antes mencionado en el Hospital Universitario desde 1959.

Material y Métodos

Revisamos retrospectivamente los expedientes médicos de los pacientes que fueron sometidos a constricción quirúrgica de la arteria pulmonar en el Hospital Universitario, desde fines del año 1959 hasta diciembre de 1970.

En nuestra serie de 80 pacientes, 39 fueron hembras y 41 varones. De este total, 48 tenían comunicación interventricular como única anomalía cardíaca. Los 32 pacientes restantes presentaban otras anomalías asociadas, que en muchos casos necesitaron procedimientos quirúrgicos adicionales, además de la constricción de la arteria pulmonar. En 19 pacientes se ligó el ducto arterioso patente y en dos de éstos además se creó una ventana interatrial. En 6 pacientes se corrigió la coartación de la aorta, 4 de ellos pertenecen al grupo que se les ligó el ducto.

Para conveniencia de la presentación y discusión, la serie se divide en dos grupos (Tabla I).

El grupo I incluye 48 pacientes con defecto interventricular aislado, más 13 con defecto interventricular y ducto arterioso patente asociado. El 50 por ciento tenían menos de 6 meses al momento de la intervención y el 80 por ciento por debajo de un año de edad.

La selección de 45 pacientes para constricción quirúrgica se hizo basada en diagnóstico clínico y no se llevaron a cabo estudios de angiocardiógrafía ni cateterismo, pues no disponíamos de laboratorio cardiovascular en esa época.

Todos los pacientes se presentaron con fallo cardíaco congestivo, soplo holosistólico rudo en el tercer y cuarto interespacio paraesternal izquierdo, retumbo diastólico apical y segundo sonido pulmonar aumentado. Infecciones respiratorias severas y repetidas, complicaron el fallo cardíaco. El tratamiento médico usual con digital, diurético, oxígeno y antibióticos, no resultó suficiente para controlarlo.

La radiografía de tórax demostró cardiomegalia con agrandamiento de ambas cámaras ventriculares, agrandamiento de atrio izquierdo, arteria pulmonar dilatada y flujo pulmonar aumentado (Fig. 1A).

El electrocardiograma demostró hipertrofia biventricular en 92 por ciento de los pacientes de este grupo con evidencia de agrandamiento de atrio izquierdo (Fig. 2A).

La mayoría de los pacientes demostraban retardo del crecimiento y malnutrición severa, encontrándose el 72 por ciento de ellos por debajo de la tercera percentila en la curva ponderal.

En 16 pacientes que se operaron a partir del 1966 se hizo estudios de cateterismo cardíaco y angiocardiógrafía. En estos encontramos que la razón del flujo pulmonar a sistemático varió de 2:1 a 7:1, con un promedio de 4:1. La presión de arteria pulmonar varió entre 38 milímetros de mercurio a 76 milímetros de mercurio con un promedio de 60 milímetros, siendo en todos los casos 50 por ciento o más, de la presión sistémica.

El grupo II (Tabla I) está compuesto por 19 pacientes con anomalías cardíacas más complicadas, la mayoría de los cuales necesitaron otros procedimientos quirúrgicos. El 80 por ciento de los pacientes de este grupo tenía menos de 6 meses de edad al tiempo de la operación. Hay en este grupo dos pacientes con transposición completa de los grandes vasos y defecto interventricular; cuatro con tronco arterioso persistente; dos con canal atrioventricular común; seis con coartación preductal de la aorta y cortocircuito de izquierda a derecha a nivel ventricular; dos con Taussig-Bing; uno de atresia tricuspídea con flujo pulmonar aumentado (tipo 1 C) y uno con cor biloculare.

Al igual que en el grupo I, estos pacientes estaban en fallo cardíaco congestivo, el cual no respondía al tratamiento médico aceptado. El 60 por ciento estaba por debajo de la tercera percentila en la curva de crecimiento. La radiografía de tórax demostraba cardiomegalia con flujo pulmonar muy aumentado (Fig. 3A). El electrocardiograma varió según las anomalías específicas. El 50 por ciento tuvo evidencia de hipertrofia ventricular derecha aislada; el 32 por ciento manifestó hipertrofia ventricular combinada y el 18 por ciento hipertrofia izquierda

TABLA I

GRUPO I			GRUPO II								TOTAL PACIENTES	% MUERTOS
EDAD	CIV-CIV + DAP		TGV	CoA + CIV	TROMCO	TAUSSIG BING	CANAL A-V	COR BILOCULARE	TRANSPOSICION CORREGIDA	ATRESIA TRICUSPIDEA		
0-2 MESES	PTES	12	1	4	1		1	1			20	45%
	•	3		4	1		1					
3-5 MESES	PTES	18	1	2	1		1		1	1	25	40%
	•	5		1	1		1		1	1		
6-8 MESES	PTES	10									10	20%
	•	2										
9-12 MESES	PTES	9									9	11.1%
	•	1										
>12 MESES	PTES	12			2	2					16	18.7%
	•	3										

NOTA:

CIV = COMUNICACION INTERVENTRICULAR
 DAP = DUCTO ARTERIOSO PATENTE
 TGV = TRANSPOSICION DE LOS GRANDES VASOS
 CoA = COARTACION DE AORTA
 • = MUERTOS

A

B



Fig. 1A y B: A- Radiografía de tórax de un paciente con defecto interventricular antes de la constricción quirúrgica de la arteria pulmonar. Demuestra cardiomegalia masiva y flujo pulmonar aumentado. B- El mismo paciente un año y medio después de poner la banda. Radiografía de tórax con cardiomegalia mínima, cono pulmonar prominente y flujo pulmonar normal.

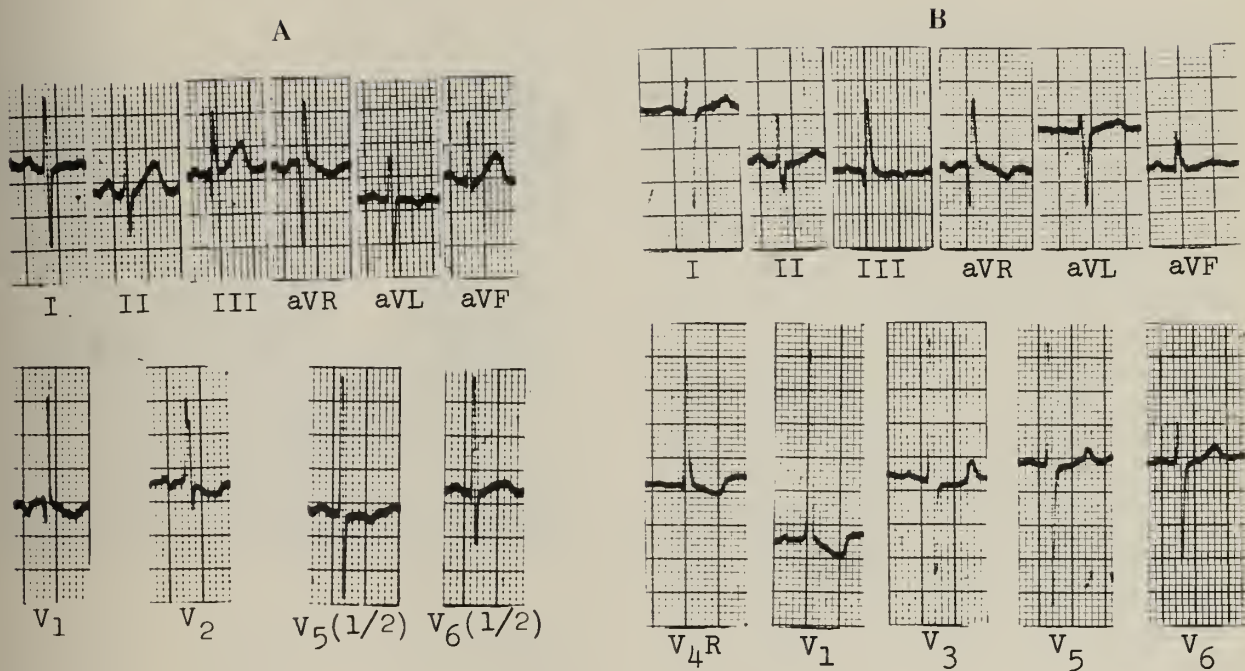


Fig. 2A y B: A- Electrocardiograma de un paciente con defecto interventricular antes de la constricción quirúrgica. B- Electrocardiograma del mismo paciente, 4 años después de la operación, demuestra hipertrofia marcada de ventrículo derecho con eje eléctrico desviado a la derecha.



Fig. 3A y B: A- Paciente con tronco arterioso tipo I, postrado en cama y en cámara de oxígeno, antes de la constricción quirúrgica. B- El mismo paciente 3 meses después de la operación paliativa, activo y haciendo vida casi normal.

solamente. En la mayoría de esos casos se confirmó el diagnóstico por cateterismo y/o angiocardiografía.

La operación consistía en colocar una cinta de hiladillo (umbilical tape), alrededor de la arteria pulmonar, reduciendo su tamaño aproximadamente a una tercera parte de su diámetro original. La efectividad de la constricción era juzgada por la presencia de un frémito en el área de la banda, disminución en tensión de la arteria pulmonar distal y disminución en tamaño y tensión del atrio izquierdo. En todos los casos, menos en uno, se exploró y ligó el conducto o ligamento arterioso.

Resultados

Grupo I:

Hubo 47 sobrevivientes en ese grupo, los cuales se han venido re-evaluando periódicamente en nuestras clínicas por un período de seis meses a diez años.

La constricción quirúrgica de la arteria pulmonar controló el fallo cardíaco en todos estos pacientes que no habían respondido al tratamiento conservador con digital, diuréticos y oxígeno.

Todos los pacientes desarrollaron un soplo eyectivo en el foco pulmonar, en muchos casos acompañado de frémito. El retumbo apical desapareció y se pudo discontinuar el digital en todos, entre uno a tres años después de la cirugía paliativa. La incidencia de infecciones respiratorias y de admisiones al hospital, disminuyó dramáticamente. La curva de crecimiento mejoró en 75 por ciento de los pacientes (Tabla II). En los casos en que no ocurrió así, se encontraron otras causas que lo explicaron, tales como hipotiroidismo en un paciente, parasitosis masiva y malnutrición debido a un medio ambiente extremadamente pobre en dos, problemas renales en uno y Hirshprung en otro.

La radiografía de tórax demostró disminución de la silueta cardíaca (Fig. 1B), disminuyendo de tamaño el ventrículo izquierdo, mientras el derecho se hacía más prominente. La vascularidad pulmonar se redujo, observándose, además, aumento en el cono pulmonar.

Dos a tres años después de la constricción, los pacientes desarrollaron hipertrofia significativa de ventrículo derecho, con patrón de sobrecarga sistólica (Fig. 2B). En el 60 por ciento de los pacientes, el electrocardiograma demostró hipertrofia aislada de ventrículo derecho y en el 40 por ciento hipertrofia combinada. Seis pacientes (10 por ciento) desarrollaron evidencia electrocardiográfica de agrandamiento de atrio derecho.

A 31 pacientes de este grupo I, se les hizo cateterismo cardíaco y angiocardiografía después de 4 a 9 años de la cirugía paliativa. Encontramos en tres pacientes que el defecto interventricular se cerró espontáneamente. El 90 por ciento de los pacientes demostraron presión elevada en el ventrículo derecho, variando entre 75 y 100

TABLA II: ESTADO NUTRICIONAL ANTES Y DESPUES DE LA CONSTRICCION QUIRURGICA DE LA ARTERIA PULMONAR EN 47 PACIENTES SOBREVIVIENTES DEL GRUPO I (TABLA I)

Percentila	↓ 3	3 - 50	↑ 50
Antes de la Constricción	35 (75 0/o)	10 (21 0/o)	2 (4 0/o)
Después de la Constricción	9 (19 0/o)	22 (47 0/o)	16 (34 0/o)

por ciento de la presión sistémica. El gradiente a través de la constricción fue de más de 45 milímetros de mercurio en todos los casos, excepto en tres que varió de 13 a 17 milímetros solamente. El gradiente más alto fue de 125 milímetros de mercurio en uno de los pacientes a quien se le había cerrado el defecto interventricular. En todos los pacientes, excepto aquellos en que se había cerrado el defecto, se demostró un corto circuito de izquierda a derecha. En una tercera parte de los pacientes se detectó un corto circuito de derecha a izquierda, ya fuera por oximetrías o por angiocardiografía. Todos los pacientes tenían una resistencia vascular pulmonar entre los límites normales.

La angiocardiografía demostró constricción de la arteria pulmonar a nivel de la banda, acompañada de dilatación post-estenótica (Fig. 4).

Mortalidad Grupo I:

En ese grupo tuvimos seis muertes en el período postoperatorio temprano, resultando una mortalidad operatoria de 10 por ciento y ocho muertes tardías, aumentando la mortalidad total a 23 por ciento (Tabla I). La autopsia en estos pacientes confirmó la presencia de un defecto interventricular grande.

Las muertes tempranas se debieron a complicaciones pulmonares y sepsis. Uno de los pacientes tenía fibroelastosis, además del defecto interventricular. De las muertes tardías, una se debió a rotura de la arteria pulmonar a nivel de la banda. Este fue el único paciente en que se había utilizado una banda con material radioopaco para hacer la constricción. Un paciente murió de neumonía y fallo cardíaco seis meses después de la constricción quirúrgica. La autopsia demostró un ducto arterioso patente significativo que pasó inadvertido durante el procedimiento quirúrgico. Otro paciente que



Fig. 4: Angiocardiograma de paciente con constricción quirúrgica de la arteria pulmonar, varios años después de la operación. Vemos el área de constricción muy marcada, con dilatación post-estenótica llamativa. Se aprecia el material de contraste pasando de derecha a izquierda, a través de la comunicación interventricular.

murió 20 meses después, se encontró que tenía fibroelastosis, además del defecto interventricular. Dos murieron con gastroenteritis, deshidratación y sepsis. Un paciente murió de várices esofágicas sangrantes. Uno más, de absceso cerebral, cinco años después de la constricción quirúrgica. La octava muerte ocurrió en otro hospital y no se le hizo autopsia al paciente.

Cirugía Correctiva:

A 28 pacientes se les ha hecho cirugía correctiva. En casi todos ellos hubo que corregir el estrechamiento de la arteria pulmonar usando un parche de pericardio. En cuatro pacientes en que la banda estaba muy cerca de la válvula, esta se encontró engrosada y deforme. El tamaño del defecto interventricular varió de 5 a 25 milímetros de diámetro. Cuatro de esos pacientes murieron. Uno de ellos murió con sepsis por pseudomonas. Otro tenía además del defecto interventricular, un drenaje anómalo de las venas pulmonares derechas al atrio derecho sin comunicación interatrial, lo cual prolongó la cirugía. Otro de los pacientes tenía estenosis residual en el infundíbulo, lo cual se cree contribuyó a la causa de muerte.

Grupo II;

Este grupo comprende aquellos pacientes con ano-

malías cardíacas más complicadas y por tanto, el grupo de más alto riesgo.

Los dos pacientes con transposición de los grandes vasos mejoraron marcadamente de su fallo cardíaco congestivo, luego de creárseles una ventana interatrial y hacer la constricción en la arteria pulmonar. Su curva de crecimiento mejoró hasta hacerse casi normal.

En los pacientes con malformación de Taussig-Bing se controló el fallo cardíaco, hasta el punto que en ambos se pudo discontinuar el digital. Su curva de crecimiento al momento es normal.

En los dos sobrevivientes con tronco arterioso persistente se controló el fallo cardíaco y se pudo discontinuar el uso de digital inmediatamente (Fig. 3B).

El único sobreviviente del grupo con coartación preductal de la aorta y defecto interventricular, ya tiene año y medio de operado. Este paciente sufrió a los siete meses de edad, endocarditis bacteriana que fue tratada con éxito. Su curva de crecimiento es muy lenta, manteniéndose por debajo de la tercera percentila.

Mortalidad Grupo II:

La mortalidad de este grupo es de 58 por ciento (Tabla I). Casi todos murieron en la sala de operaciones o poco después. Algunos de los pacientes estaban moribundos al momento de llevarlos a operar.

Los dos pacientes con canal atrioventricular común murieron en el período postoperatorio tardío, debido a sepsis. El paciente con transposición corregida murió seis meses después de la constricción quirúrgica, con una miocarditis viral. Dos pacientes con tronco arterioso persistente, murieron durante la cirugía; ambos tenían menos de seis meses de edad. De los pacientes con coartación de la aorta, murieron cinco; todos en el período postoperatorio inmediato excepto uno que murió tres meses después de la cirugía con neumonía y sepsis. La autopsia en uno de ellos reveló, además, canal atrioventricular y estenosis subaórtica.

Discusión

La mortalidad en infantes con defecto interventricular que desarrollan fallo cardíaco congestivo es muy alta. En una serie publicada por Morgan, Griffith y Blumenthal (14), de 125 niños con defecto interventricular, 17 desarrollaron fallo cardíaco congestivo antes de los seis meses de edad, de los cuales 10 murieron antes del año de vida.

En un esfuerzo por disminuir esta mortalidad tan elevada, en 1952 Muller y Damman (1) introdujeron la constricción quirúrgica de la arteria pulmonar, como

método paliativo para disminuir el flujo excesivo a los pulmones y prevenir el desarrollo de hipertensión pulmonar vascular. Posteriormente se ha utilizado este método, en otras anomalías más complicadas, asociadas con un corto circuito de izquierda a derecha a nivel ventricular, tales como ventrículo único, canal atrio-ventricular, tronco arterioso persistente y atresia tricuspídea con flujo pulmonar aumentado (tipo I-C). La transposición completa de los grandes vasos, y coartación preductal de la aorta, cuando están asociados a un defecto interventricular, también se benefician de este procedimiento.

Como se ha informado en otras series y hemos podido observar en nuestros propios pacientes, luego de la constricción quirúrgica de la arteria pulmonar, se controla el fallo cardíaco congestivo, se disminuye marcadamente la frecuencia de infecciones pulmonares y la curva de desarrollo se hace normal en la mayoría de los casos. La cirugía correctiva puede hacerse entonces en forma electiva, en un paciente en condiciones óptimas desde el punto de vista médico.

En pacientes con anomalías complicadas, en cuyos casos la cirugía correctiva es aún muy difícil o imposible, les mejora de sus síntomas y les dá la oportunidad de beneficiarse en el futuro de los rápidos avances de la técnica quirúrgica.

Aunque no se ha probado definitivamente que esta operación cause regresión de los cambios vasculares pulmonares, relacionados a la hipertensión pulmonar, Damman (15) ofrece evidencia patológica de regresión de cambios vasculares observada en pacientes con defecto interventricular e hipertensión pulmonar que fueron sometidos a este procedimiento. Sin embargo, este concepto no es aceptado por algunos grupos (16). Todos nuestros pacientes tenían resistencias pulmonares normales al momento de la cirugía correctiva, aún cuando clínicamente se había considerado, en algunos casos, la presión pulmonar elevada al momento de la cirugía paliativa.

Es difícil de adivinar qué curso hubiesen tomado nuestros pacientes, de no habérseles creado la constricción quirúrgica. Indudablemente muchos habrían muerto de insuficiencia cardíaca o neumonía y otros habrían desarrollado hipertensión pulmonar irreversible. Sabemos que en tres casos (5 por ciento del grupo I) el defecto interventricular se cerró espontáneamente. Esto también ha sido informado en otros centros (17-18). Aunque de 25-30 por ciento de todos los defectos interventriculares se cierran espontáneamente, esto es más raro en los defectos grandes (19), como es el caso de los pacientes que se someten a constricción quirúrgica de la arteria pulmonar.

gica de la arteria pulmonar.

El procedimiento sin embargo, no está libre de riesgos. La mortalidad es mayor en los pacientes menores de seis meses, especialmente cuando hay anomalías asociadas. (Tabla I). La mortalidad del procedimiento informada por otros centros de Estados Unidos e Inglaterra, varía de 10 - 55 por ciento. En pacientes con anomalías severas, la mortalidad informada es de 33 - 70 por ciento.

Uno de nuestros pacientes murió repentinamente luego de perforarse la arteria pulmonar en el sitio de la banda. Hunt *et al* (7) e Idriss *et al* (11), también informan casos similares. Osborn *et al* (20) y Lynfield *et al* (21) informan trombosis en la arteria pulmonar proximal, secundaria a un área de necrosis del vaso en el área de la banda. También han sido informados casos en que la banda ha cortado la pared del vaso, el cual se ha sellado sobre aquella. Durante la cirugía correctiva se encontró la banda dentro del lumen del vaso (11, 22).

En el curso natural de un paciente con constricción quirúrgica de la arteria pulmonar, esta área se va quedando pequeña, mientras el resto del corazón sigue creciendo. El gradiente a través de la banda se hace mayor, se hipertrofia el ventrículo derecho, en muchos casos afectando el área del infundíbulo. Algunos pacientes desarrollan corto-circuito bidireccional a través del defecto. Esto ocurrió en una tercera parte de nuestros pacientes, dejando ver que esos cambios puedan alterar la mortalidad a largo plazo. Uno de ellos murió a causa de un absceso cerebral relacionado con corto-circuito de derecha a izquierda. En uno de los pacientes que murió luego de cirugía correctiva, se encontró una obstrucción a nivel infundibular, que indudablemente estuvo relacionado con la causa de la muerte.

Otra complicación informada con relativa frecuencia en otras series es el engrosamiento y deformidad de la válvula pulmonar cuando la banda está muy cerca de ésta. En nuestra serie, aún cuando se identificó en algunos casos, no causó problema.

Aunque perdimos cuatro pacientes entre los primeros en someterse a cirugía correctiva, se debió principalmente a fallas técnicas que han sido corregidas. En la actualidad la mortalidad del procedimiento final es muy baja en nuestra institución, al igual que en otros centros (7, 11, 23).

En resumen, a pesar de los riesgos envueltos, este puede ser un procedimiento sumamente beneficioso cuando está indicado. Para la constricción quirúrgica de la arteria pulmonar, consideramos a los infantes menores de un año con corto-circuito de izquierda a derecha a

nivel ventricular, en fallo cardíaco congestivo, con infecciones respiratorias severas y repetidas resistentes al tratamiento médico vigoroso, unido a un crecimiento físico muy lento.

Es importante que la cirugía correctiva se lleve a cabo dentro de los próximos 2 a 4 años después de la paliativa, para evitar la mayoría de las complicaciones antes descritas.

Resumen

Presentamos un análisis de 80 pacientes sometidos a constricción quirúrgica de la arteria pulmonar de los cuales el 60 por ciento tuvieron defecto interventricular aislado y el 40 por ciento otras anomalías cardíacas asociadas.

Se describen los hallazgos físicos, electrocardiográficos y radiográficos pre y postoperatorios, así como los de cateterismo y angiocardigrafía. Además se describen los hallazgos operatorios en aquellos pacientes que han sido sometidos a cirugía correctiva.

Se discuten los resultados, mortalidad y complicaciones de los procedimientos paliativo y correctivo. Hacemos recomendaciones en cuanto a las indicaciones para la constricción quirúrgica de la arteria pulmonar y el tiempo en que se debe llevar a cabo la cirugía correctiva.

Summary

Eighty patients who have undergone pulmonary artery banding at the University Hospital are presented. Sixty percent of the cases had isolated ventricular septal defect and forty percent had other associated cardiac anomalies.

We describe the physical, electrocardiographic, and roentgenographic findings before and after the procedure, as well as the cardiac catheterization and angiography. The operative findings and results in 26 patients who have undergone complete repair are reviewed.

The results, mortality, and complications of the palliative and of the corrective surgery in our series, as well as in those reported in the literature, are discussed.

Recommendations are made regarding the indications for pulmonary artery banding and the time of complete repair.

Reconocimiento

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MARCAPASOS EN NIÑOS: *Diez Años de Experiencia Clínica*

Mercedes Vega Vidal, MD

La estimulación artificial eléctrica del músculo cardíaco es hoy día una forma de tratamiento para pacientes con problemas en el sistema de conducción.

En niños, la indicación primaria para el uso de marcapaso es la prevención de las crisis sincopales que acompañan al paro circulatorio en pacientes con bloqueo aurículoventricular persistente. A pesar de que el uso de marcapasos ha logrado disminuir grandemente la morbilidad y mortalidad en pacientes con bloqueo aurículoventricular sintomático, los problemas que esos dispositivos acarrearán son frecuentes, y en algunos casos, graves. Ello complica el seguimiento a largo plazo de estos pacientes.

Relataremos aquí nuestra experiencia con marcapasos en el tratamiento de niños que tienen bloqueo aurículoventricular.

Metodología

Durante el período que comprende desde enero de 1960 hasta diciembre de 1970, se trataron y evaluaron a un total de once niños con marcapasos.

Revisamos sus historias clínicas (Tablas I - II). La serie consta de 6 niñas y 5 varones, sus edades fluctuaban entre dos a once años al momento del diagnóstico, y entre los dos hasta los doce años al implantárseles el primer marcapaso.

El bloqueo aurículoventricular pareció ser congénito en siete casos por descubrirse antes de los dos años de edad. En un paciente había duda sobre la etiología porque se encontró a los seis años de edad. La causa del bloqueo en los tres restantes fue secundario a infecciones virales del miocardio. Ninguno mostró una incidencia familiar de este trastorno del ritmo.

En un paciente la indicación para implantar el marcapaso no fue claramente definida, el resto presentó síntomas debido a un volumen minuto bajo. Ocho de los once casos desarrollaron el Síndrome de Adams-Stokes (Tabla I). Sólo un paciente presentó anomalías cardíacas asociadas. Estas se corrigieron quirúrgicamente al año de haberse establecido el diagnóstico del bloqueo aurículoventricular (Tabla II). Después de confirmado el diagnóstico y en vista de la sintomatología, cada

paciente recibió un marcapaso transitorio previo a la implantación del marcapaso permanente.

El electrodo del marcapaso transitorio se introduce por vía endovenosa, bajo control fluoroscópico hasta el ventrículo derecho. Contenidos en una sonda, los electrodos se colocan cerca de la punta del ventrículo derecho, dentro de las trabéculas musculares. Los dos cables exteriores del electrodo se conectan a un generador externo de frecuencia fija. Tanto la frecuencia como la intensidad del estímulo eléctrico pueden gobernarse manualmente.

La técnica de implantación del marcapaso permanente depende del tipo de electrodo a usarse: epicárdico o intracavitario. Todos los pacientes recibieron un marcapaso permanente con un generador de frecuencia fija y electrodos epicárdicos excepto uno (Tabla I - Núm. 6), que recibió un electrodo intracavitario. Para colocar los electrodos epicárdicos, el abordaje es por una toracotomía anterolateral izquierda. Se suturan los electrodos a la pared epicárdica y se llevan los cables hasta el área subcostal izquierda dentro de un túnel subcutáneo donde se conectan al generador localizado en un bolsillo debajo de la piel. El generador también se puede colocar bajo el pectoral mayor. Al confirmarse la función del marcapaso permanente, se retira el marcapaso transitorio. El paciente recibe antibióticos profilácticos rutinariamente.

Implantado el marcapaso, todos los pacientes se siguieron con electrocardiogramas y radiografías de tórax y abdomen.

Resultados

Los síntomas preoperatorios desaparecieron en todos nuestros pacientes. Llevan una vida activa, sin excluir los juegos propios de su edad. La cardiomegalia mejoró o desapareció. Los electrocardiogramas demuestran una frecuencia ventricular constante. Cada complejo QRS es precedido por una línea vertical que corresponde a la señal del marcapaso (Fig. 1).

Durante el período de seguimiento de estos casos, que varió desde uno hasta seis años, se reemplazaron el cable electrodo y el generador en varias ocasiones. A un paciente (Tabla I -- Núm. 5), se le cambió el sistema por uno de demanda.

Fue necesario un total de 49 intervenciones quirúrgicas para corregir las fallas encontradas en los marcapasos (Tabla III). De las 49 fallas, 12 fueron por baterías agotadas; 4 por desperfectos en el generador (run-away battery); 15 por rotura del cable; en uno, el electrodo epicárdico se partió; en otra, el electrodo

TABLA I: DATOS GENERALES

Paciente	Sexo	Diagnóstico Edad Paciente en Años	Marcapasos Edad Paciente en Años	Años de Seguimiento	Muertes	Adams Stokes	Mareos	Tolerancia Pobre Ejercicio
1	F	2	4	5				x
2	M	1/12	6 1/2	5		x		
3	F	2 1/2	9	5		x		
4	F	2	2	-	x	x		
5	M	6	7	6		x		
6	M	11	12	3			x	
7	M	5	5	6		x		
8	F	6	8	-	x	x		
9	F	5	5	1		x		
10	F	2 1/2	2 1/2	5		?	?	?
11	M	5	11	2 1/2				x

Los pacientes de esta serie no presentaron Insuficiencia Cardíaca Aguda.

TABLA II: CLASIFICACION ETIOLOGICA

<i>Congénita</i>	
Con anomalías cardíacas asociadas	1
Sin anomalías cardíacas asociadas	7
<i>Adquirida</i>	3
Total	11

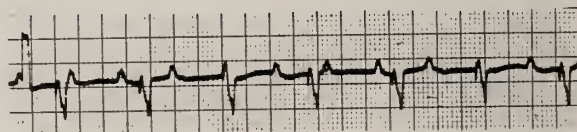


Fig. 1: Derivación II ECG demostrando señal del marcapaso que corresponde a la línea vertical que precede cada QRS.

TABLA III: COMPLICACIONES

<i>1. Generador:</i>	
Infecciones	3
Necrosis cutánea	3
Hematomas	1
Re-ajuste frecuencia	1
Baterías agotadas	12
Generador descontrolado ("run-away battery")	4
<i>2. Reemplazo Cable-electrodo:</i>	
Epicárdico-intracavitario	3
Intracavitario-intracavitario	4
<i>3. Electrodo:</i>	
Rotura	2
Re-posicionar	1
<i>4. Cables Rotos</i>	15
5. TOTAL FALLA EN 7* PACIENTES:	49

* Se excluyen 2 pacientes muertos y 2 pacientes que no han tenido complicaciones aún.

intracavitario se rompió al nivel de la válvula tricuspídea; en otra el electrodo intracavitario se relocalizó; y en siete ocasiones fue menester reemplazar el cable electrodo. En un caso hubo que reajustar la frecuencia del generador. Seis pacientes desarrollaron infecciones, y uno, hematoma localizado al área donde se encontraba el generador.

Hay un paciente (Tabla I -- Núm. 1), cuyo generador tiene las baterías agotadas y los cables rotos, pero los padres han rehusado que se implante un nuevo marcapaso. La niña está asintomática a pesar de que tiene un pulso de 44 por minuto. Su electrocardiograma aún demuestra bloqueo con ritmo idioventricular variable de 40-50 por minuto.

En esta serie ocurrieron dos muertes. Ambas niñas sufrían de bloqueo auriculoventricular adquirido. Sus padres rechazaron el marcapaso cuando se les propuso. Más tarde, estas pacientes fueron recluidas con crisis sincopales graves y frecuentes. Se intentó entonces ponerles el marcapaso transitorio, pero sin éxito. Una desarrolló fibrilación ventricular y la otra, taquicardia ventricular, durante el procedimiento.

Discusión

Normalmente el estímulo intrínseco del corazón se origina en el nodo sinusal y se propaga por las aurículas hasta el nodo atrioventricular. Sigue por el fascículo de His, pasa a sus dos ramas principales hasta propagarse por todo el tejido ventricular. En los casos de bloqueo aurículoventricular total, el estímulo no se propaga a los ventrículos. Las aurículas y los ventrículos trabajan independientemente. El estímulo eléctrico intrínseco que activará los ventrículos se pueden originar en el nodo atrioventricular, el fascículo de His o cualquiera de sus ramas. Mientras más bajo en el ventrículo sea el foco activador, más lenta será la frecuencia del estímulo ventricular.

Las ondas P en el electrocardiograma aparecen según el ritmo sinusal, mientras que el complejo QRS sigue al foco secundario. Por consiguiente, se pierde la relación normal entre las ondas P y el complejo QRS. En ocasiones, hay una aparente relación normal, pero ello se debe a que coinciden al azar en un momento dado.

En el bloqueo aurículoventricular de los niños, ninguno de los dos sexos predomina (1, 2). El bloqueo puede ser de origen congénito o adquirido. Si es congénito, puede ser secundario a infecciones intrauterinas con formación de tejido cicatricial a lo largo del sistema de conducción, o debido a un desarrollo incompleto de este sistema. Algunos autores (3-8) han informado series de casos donde se implica al factor hereditario en la etiología del bloqueo aurículoventricular.

Las causas del bloqueo aurículoventricular adquirido son numerosas. Con los adelantos de la medicina, las propiamente médicas han disminuído, pero, simultáneamente, la incidencia de bloqueo secundario a la cirugía intracardiaca ha aumentado.

Se han descrito anomalías cardíacas asociadas (2, 3, 9, 10). La transposición corregida de los grandes vasos y el canal atrioventricular común son las más frecuentes. En nuestra serie, sólo un paciente tuvo anomalías cardíacas asociadas, comunicación inter-auricular, retorno anómalo de las dos venas pulmonares derechas al atrio derecho y rotación del hígado al lado izquierdo. En 1929 (11), se informó un caso de bloqueo aurículoventricular asociado a un defecto congénito cardíaco y heterotaxia parcial de las vísceras abdominales.

En los jóvenes con bloqueo aurículoventricular sin otras anomalías asociadas, el cuadro clínico está determinado por la capacidad que tiene el miocardio de mantener un gasto cardíaco adecuado por medio de un aumento en el volumen minuto, a pesar de la bradicardia existente, lo mismo durante el ejercicio que en el reposo (9, 12).

No siempre los pacientes compensan adecuadamente. Por consiguiente, al disminuir el volumen minuto, el gasto cardíaco disminuye en algunos y resulta en una insuficiencia circulatoria cuya sintomatología varía según la gravedad (1, 2). El síncope, aunque raro en los niños, (2, 6, 10, 13, 14, 15) es lo más ominoso en un paciente con bloqueo aurículoventricular.

Las crisis sincopales (Adams-Stokes) son desmayos asociados con un pulso lento y persistente, por lo general alrededor de 40 por minuto. En la mayoría de los casos la pérdida de conocimiento ocurre durante las variaciones de ritmo secundarias a cambios súbitos del foco donde se origina el estímulo ventricular. Puede ocurrir asistolia, fibrilación, taquicardia ventricular, o una combinación de estas arritmias. La pérdida del conocimiento es brusca, sin signos prodrómicos. Al recuperarlo, el paciente suele mostrar poca confusión o pocos residuos postsincopales.

Estos episodios, si son breves, no más de tres o cuatro segundos de duración, sólo producen pérdida del conocimiento en posición erecta. Hay casos con duración prolongada del período de asistolia. En este grupo de pacientes observamos manifestaciones neurológicas tales como movimientos convulsivos, midriasis, y confusión prolongada.

Las crisis sincopales pueden recurrir varias veces al día, no guardan relación alguna con la actividad del paciente al momento del episodio, ni con la posición, y pueden ocasionar una muerte súbita, (2, 4, 8, 16) si los ventrículos no logran volver a contraerse eficazmente antes de que produzcan la lesión cerebral.

En niños, el tratamiento del bloqueo aurículoventricular depende de que haya o no síntomas. En los casos asintomáticos, el paciente no recibe tratamiento alguno. La mayoría de estos niños llega a la edad de adulto sin complicaciones (9, 10, 16, 17). Tan pronto existen síntomas relativos a la arritmia, (2, 18) el paciente debe recibir tratamiento adecuado para mejorar su gasto cardíaco lo antes posible y evitar complicaciones graves. Se ha recomendado el uso de Isoproterenol (Isuprel) para la aceleración de la frecuencia cardíaca pero los resultados a largo plazo son bien pobres.

Aunque el empleo de electricidad en terapéutica no es nada nuevo, no fue hasta hace aproximadamente veinte años que Zoll (19) logró reanimar el latido cardíaco de pacientes con paro circulatorio, usando acertadamente estímulos eléctricos extrínsecos.

En esta nueva técnica se ha progresado significativamente. Hoy contamos con electrodos que estimulan directamente al músculo cardíaco y con generadores livianos de fácil manejo. En el 1960 (20), se logró

implantar satisfactoriamente el sistema en uso actualmente, es decir, un marcapaso electrónico compacto instalado debajo de la piel.

El estímulo eléctrico se origina en un circuito electrónico pequeño donde la energía la suple una serie de baterías. Ocurre en éstas una reacción electroquímica donde el óxido de mercurio se reduce a mercurio. El mercurio a su vez se deposita gradualmente en las placas de las baterías. Este generador está sellado con un material inerte que lo protege de los tejidos y sus posibles reacciones químicas.

El estímulo va directamente desde el generador al electrodo insertado en el epicardio o fijo en las trabéculas musculares del ventrículo derecho (Fig. 2), por un cable sellado e igualmente protegido por un material inerte.

Hoy día, existen diferentes tipos de marcapasos, (21, 22, 23) los cuales difieren en sí por la forma que originan la contracción ventricular y en la posición de los electrodos. Nuestros pacientes recibieron el marcapaso con generador de frecuencia fija y electrodos epicárdicos. En un paciente, nada más, usamos un electrodo intracavitario inicialmente. Las ventajas y desventajas de un electrodo sobre otro han sido discutidas por otros autores, (24, 25) al igual que las de los generadores de frecuencia fija y frecuencia sincronizada.

Aunque las indicaciones para el uso del marcapaso son varias (26), la indicación primaria en niños es en la prevención de Adams-Stokes.

La configuración de los complejos QRS puede variar en un mismo paciente, antes y después de insertarse el marcapaso (Fig. 3). Tales variaciones se deben al nivel de implantación de los electrodos en el epicardio, y, por consiguiente, al punto de origen del estímulo ventricular.

Como el marcapaso es un sistema de componentes, es de esperar que, de haber complicaciones, éstas ocurran por fallas de uno de esos componentes: perforaciones del ventrículo por el electrodo intracavitario, efectos directos del medio ambiente (20, 27, 28) sobre el marcapaso (ondas de radio, electromagnéticas y ultrasónicas, diatermia, etc.), además de, infecciones (29) y rechazo del cuerpo a una sustancia extraña. Las complicaciones que hemos encontrado en nuestra serie (Tabla III), no difieren de las descritas en la literatura excepto, quizás, por la alta incidencia de trauma como factor precipitante. Esto se debe al tipo y grado de actividad que llevan nuestros pacientes. Igualmente, la incidencia de infecciones (12 por ciento) es alta. Es interesante observar que cinco de los seis episodios de infecciones ocurrieron con el generador localizado al área del pectoral mayor (Fig. 4).

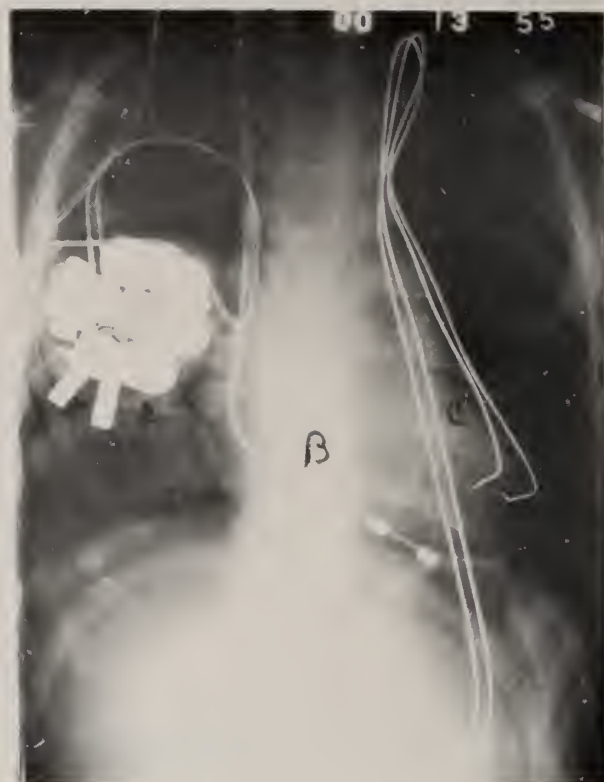


Fig. 2: Radiografía de tórax en posición postero-anterior demuestra el generador (A) localizado en el área sub pectoral derecha y conectado a un cable electrodo (B) bipolar intracavitario. (Obsérvese la punta de este último hacia el ápice del ventrículo derecho). También podemos ver otro cable electrodo (C) epicárdico bipolar. Estos forman en su punta una angulación de 90° . Es esta el área que se inserta en el corazón. Nótese que el electrodo más lateral está partido.

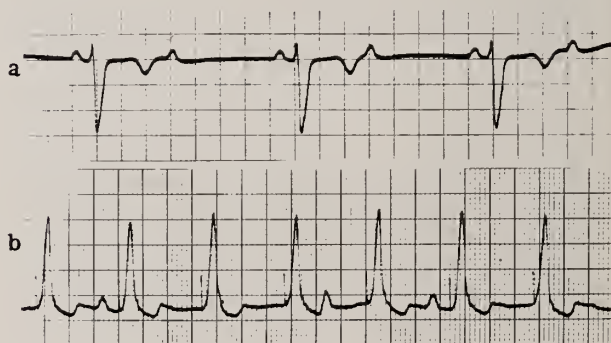


Fig. 3: Derivación II ECG: 3a) bloqueo A-V 2:1 antes de implantarse el marcapaso. 3b) Luego de implantado el marcapaso la orientación del QRS se altera. Obsérvese señal del marcapaso precediendo cada QRS.



Fig. 4: Paciente con generador localizado en el área del pectoral mayor. Obsérvese que una de las puntas del generador han perforado la piel y la otra ha causado necrosis y casi ha perforado también.

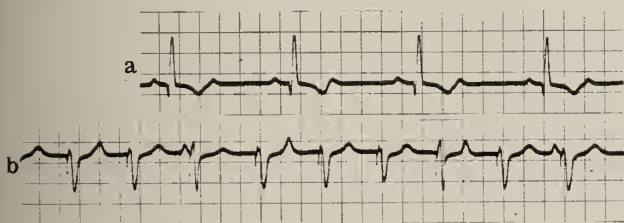


Fig. 5: Derivación II ECG de un mismo paciente tomadas una en posición supina y seguidamente en posición sentada. 5a) paciente acostado presenta ritmo idioventricular de 40/min. y ausencia total de actividad del marcapaso. 5b) paciente sentado demuestra que hay actividad del marcapaso y que lo está siguiendo a una frecuencia de 100/min.

Es importante recalcar que aunque la implantación del marcapaso resuelve ciertos problemas otros se producen debido a éste y en algunos casos, graves. Deben verse estos pacientes en la consulta externa frecuentemente; cada tres meses. El interrogatorio será minucioso, y el examen físico concienzudo; éste no olvidará la evaluación del pulso tanto en la posición acostada

como sentada (Fig. 5). Periódicamente, se deben tomar radiografías del área donde se encuentra el generador para evaluar el período de vida de las baterías (30) (Figs. 6A & B), al igual que trazados electrocardiográficos, para apreciar la respuesta del ventrículo al marcapaso (Fig. 5), la frecuencia con que dispara el generador (Fig. 7), la amplitud de la señal y la existencia o no de escape (31) (Fig. 8). A los padres de los pacientes se les debe enseñar a tomar el pulso, e instruirlos a que lo tomen diariamente. Cualquier variación ± 10 en el pulso se debe notificar.

En aquellos casos donde el historial o el examen físico sugiera dificultades, se tomará al paciente, además, una radiografía que abarque tanto el electrodo como los cables, para determinar la posición de aquél y la posibilidad de rotura de éstos (Fig. 2, 6B).

Toda falla trazada al marcapaso debe corregirse inmediatamente con la protección de un marcapaso transitorio (28), que se pondrá en uso cuando se requiera desconectar el generador de los electrodos permanentes. Por razones de seguridad para el paciente, no debe operarse ninguno sin tener ya un marcapaso transitorio. Así puede regularse el pulso según lo requiera la inducción de anestesia y el acto operatorio.

La sobrevivencia del paciente con bloqueo aurículo-ventricular depende del marcapaso implantado. El progreso futuro de este campo se concentrará en reducir el tamaño de los generadores para su uso rutinario en infantes, mejorar la calidad de los cables electrodos y aumentar la duración de las baterías.

El uso de energía nuclear o de energía derivada del paciente, junto al desarrollo de una activación del miocardio más fisiológica quizás resuelvan en gran parte, los problemas propios del implante permanente de marcapasos en niños.

Resumen

Se presenta la experiencia de diez años en el Hospital Universitario con once niños con marcapasos. Se revisan las historias clínicas. La serie consta de 6 niñas y 5 varones entre las edades de dos a doce años. En ocho de los casos el bloqueo aurículo-ventricular es congénito y en tres, es secundario a infecciones virales del miocardio. No hay incidencia familiar de este trastorno del ritmo. Sólo un paciente presentó anomalías cardíacas asociadas. Todos ellos, excepto uno, presentaron sintomatología debida a un volumen minuto bajo.

Cada paciente recibió un marcapaso transitorio pre-

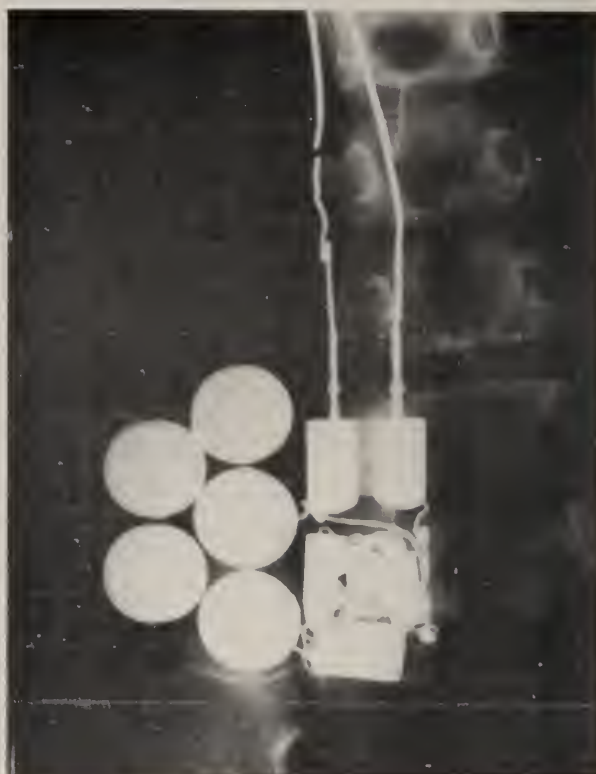


Fig. 6 (a y b): Radiografía para evaluación del período de vida de baterías. 6a) Las áreas radiolúcidas que existen en las baterías se van opacificando a medida que las baterías se agotan debido a la acumulación de mercurio en éstas. 6b) Baterías prácticamente agotadas. Obsérvese que uno de los cables está partido a varios niveles. En el nivel superior además ha ocurrido separación de los cables.

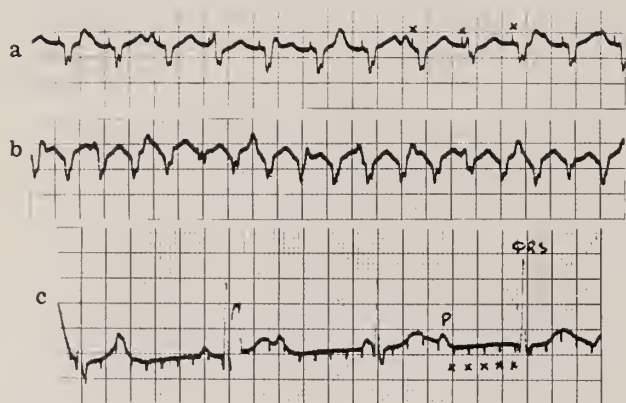


Fig. 7: Derivaciones II ECG demostrando generadores descontrolados. a) marcapaso con frecuencia de 140/min. b) marcapaso con frecuencia de 220/min. c) marcapaso con frecuencia de 500/min. pero no logra activar los ventrículos como en los mencionados previamente. Ritmo idioventricular de 60/min.

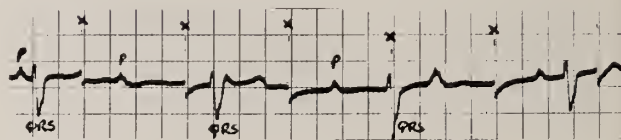


Fig. 8: Derivación II ECG demostrando escape al marcapaso. Señal marcapaso (X) no precede al QRS.

vio a la implantación del marcapaso permanente. El marcapaso usado es con generador de frecuencia fija y electrodos epicárdicos excepto en un paciente, que se usó un electrodo intracavitario. Sólo ocurrieron dos muertes y fueron éstas durante el proceso de implantarles el marcapaso transitorio, a pacientes seriamente enfermos.

Las complicaciones encontradas fueron; defectos del generador, rotura de los cables o de los electrodos, desplazamiento del electrodo, baterías agotadas, infecciones y hematomas. La falla mayor fue a nivel de los cables rotos y la incidencia más alta de complicaciones se encontró en los varones.

Summary

The hospital records of eleven children, six girls and five boys admitted to the University Hospital and in whom cardiac pacemaker implantation was performed during the years 1960 to 1970 were reviewed. The age range was from two to twelve years of age. A diagnosis of congenital complete atrioventricular block was established in eight patients and of acquired atrioventricular block secondary to viral myocarditis, in three cases. Associated congenital heart defects were described in only one patient. None of these patients showed a familial incidence. All of them presented with symptoms secondary to a low cardiac output.

Prior to the implantation of the permanent pacemaker, each patient received a temporary one. In all instances, epicardial electrodes with a fixed rate type of generator was used initially, except for one patient who received an intracavitary electrode. Two deaths are described in this series and they occurred in critically ill children.

The following complications were observed: generator defects, broken wires and/or electrodes, dead batteries, infections and a hematoma. The highest incidence of complications was found among the boys, being broken wires the most common problem.

Reconocimiento

Queremos reiterar nuestro agradecimiento a la señora Norma C. González, a la señorita Rebeca Puente y a la señora Clara N. de Aparicio, por su valiosa asistencia en la elaboración de estos artículos.

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NOTA DEL EDITOR:

Existen limitaciones en nuestro país que impiden el seguimiento óptimo del paciente con un marcapasos. Se recomienda, para determinar cuándo cambiar el generador, el uso del osciloscopio. Sería ideal una clínica únicamente para pacientes con marcapasos, y si no hay facilidades de osciloscopio, cuando el generador excede 18 a 20 meses de vida puede cambiarse electivamente o si ocurre una variación en pulso por minuto de ± 4 para Medtronic, y ± 8 para Cordis.

CARDIOLOGIA PEDIATRICA: ALCANCES EN PUERTO RICO

Las subespecialidades pediátricas han tenido, como nuevas disciplinas, un auge dramático en los últimos quince años. La Pediatría se ha convertido en una especialidad científica compleja, a la vez que nuestro conocimiento de la fisiología dinámica y patología fisiológica del ser humano en su edad temprana, ha ido en aumento.

El progreso en la Cardiología Pediátrica ocurrió cuando un grupo de médicos se dedicó exclusivamente al estudio de estas enfermedades, al comprender que su fisiopatología no seguía los conceptos establecidos en el adulto. La especialidad se desarrolló vertiginosamente y en muy pocos años ocurrieron avances trascendentales en el diagnóstico y tratamiento médico y quirúrgico de las cardiopatías en los niños. El fruto de esta ferviente actividad que contemplamos hoy es resultante del esfuerzo común de un grupo de especialistas cuyo equipo lo han integrado cardiólogos, cirujanos cardiovasculares, anestesiólogos, fisiólogos y personal paramédico especializado.

La Sección de Cardiología del Departamento de Pediatría fue establecida en el Hospital Universitario en el año 1959. Los años subsiguientes fueron testigos del desarrollo de la Sección, lento y a veces doloroso, hasta el presente, cuando se cuenta con un grupo de especialistas bien entrenados, tres de ellos aquí, personal paramédico especializado, y se vislumbran en un futuro cercano las facilidades técnicas necesarias para un servicio eficiente y un programa científico adecuado. Confiamos que la serie de artículos publicados hoy en este Boletín, sea el comienzo de dicho programa.

Amalia Martínez Picó, MD

EJEMPLO, PROBLEMAS Y PREGUNTAS

Entusiasmo sincero producen los artículos incluídos en esta edición del Boletín. Recopilan amplia experiencia adquirida a pesar de obstáculos, frustraciones, y apatía, vencidos sólo por la convicción de quienes creyeron de primordial necesidad el estudio hemodinámico y el tratamiento definitivo de pacientes pediátricos con lesiones cardíacas en el país donde nacieron.

¿Merece este esfuerzo ser señalado con orgullo? Tomemos excepción a la observación de Nemesio Canales: "Aquí los hombres de letras no se entusiasman nunca por la obra de ningún compañero, y sí se entusiasman, lo hacen con tantísima reserva que nadie se entera. Aquí somos, o nos hacemos, los indiferentes, los desdeñosos, los unos con los otros". No debe pasar inadvertido en el elogio el aspecto preventivo de suma importancia llevado a cabo en esta Sección de Cardiología Pediátrica de la Escuela de Medicina.

¿Merecen una oportunidad para comentar editorialmente aquéllos que todavía evaden sus responsabilidades al enviar fuera de su país pacientes pediátricos con lesiones congénitas! La calidad del trabajo de nuestros pediatras cardiólogos ya es innegable: canalizar pacientes innecesariamente a centros del exterior constituye una negación irracional a esta calidad indiscutible. Refugiarse detrás de

la excusa obsoleta de que las facilidades privadas existentes son insuficientes es acusarse de no haber apoyado su progreso: ¿no ha logrado lo aquí descrito el grupo del Hospital Universitario con facilidades que distan y distaron de ser óptimas? Sería ingenuo creer que lo existente allí cayó como el maná: cada cama, cada monitor, cada sonda, cada nombramiento fue luchado y obtenido por esfuerzo máximo: ¡ejemplo a emular! ¡y lo que falta por conseguir!

Preguntamos, ¿o es que existen en Puerto Rico actualmente dos "standards" en cuanto a servicios médicos en esta área, uno para pacientes indigentes y otro para pacientes privados? Por lasitud, por desinterés, por frustración, y en algunos casos por falta de información, se ha permitido que la comunidad carezca aún de medios para estudiar y tratar las enfermedades cardiovasculares aquí excepto mercedamente en centros gubernamentales. Es irónico que pacientes del sector económicamente productivo de nuestra sociedad — que con sus contribuciones sufraga las facilidades públicas — sean obligados a someterse a estudios y cirugía delicada en el exterior, atemorizados por la separación de sus familias, por lo extraño de otro país, sin tener la oportunidad de comunicarse con sus médicos en forma íntima y con continuidad. Ante el ejemplo de nuestros cardiólogos pediátras: ¿por qué no luchar para proporcionarles las mejores facilidades aquí? Ya es hora que se cuestione francamente todo esfuerzo, tanto en el plano personal, institucional o de las asociaciones benéficas. ¿Debe continuar nuestro apoyo económico a campañas donde el beneficio es a un sólo paciente, o a un sólo tipo de entidad, o deben canalizarse los fondos obtenidos para lograr facilidades que beneficien a todos?

Felicitemos nuevamente a la Sección de Cardiología del Departamento de Pediatría del Hospital Universitario. Con su labor han dado ejemplo para emular, problemas para ponderar y preguntas para contestar.

Jorge O. Just Viera, MD

NOTICIAS

News Release from the Geriatric Pharmaceutical Corporation:

Geriatric Pharmaceutical Corporation has made available prints of a 16 minute, 16 millimeter, color and sound film entitled "Decision". The film was prepared in cooperation with the Self Employment Group of APTA and selected pharmaceutical manufacturers, and was filmed at the University of California Department of Physical Medicine and Rehabilitation.

The film is tailored to students at the high school or early college level, and portrays the background and activities of the physical therapist. It follows the activity of the therapist through his professional training and practice, in the classroom, in the hospital, in the office and in the home. The film is strictly non-commercial, no products or devices are advertised or recommended.

"Decision" is of invaluable assistance to R.P.T.'s who are called upon by civic and other groups to talk about their work, since its comprehensive explanations cover virtually every facet of the profession. It can simplify and shorten the oral explanation by the R.P.T. and has been found to generate a lively "question and answer" period after its viewing.

The film is especially valuable for administrators and educators, for viewing by students who might be interested in pursuing a career in Physical Therapy.

Arrangements for booking on loan can be made by writing to Mr. Gustave Bardfeld, Director of Clinical Research, Geriatric Pharmaceutical Corporation, 397 Jericho Turnpike, Floral Park, N. Y. 11001.

The Tenth International Conference on Extra-Corporeal Technology will be held on July 27, 28 and 29, 1972, at the Waldorf-Astoria in New York City for dialysis, heart-lung, and artificial organs technologists. For inquiries write to: Edward C. Berger, Executive Director, American Society of Extra-Corporeal Technology, Inc., 287 East Sixth Street, St. Paul, Minnesota 55101.

The 32nd Annual AMA Congress on Occupational Health will be held at The Drake Hotel in Chicago, September 11-12, 1972.

The IV Medical/Legal Institute will hold a Postgraduate Medical Education Program on MEDICAL MALPRACTICE, A Legal Course for Doctors — to be held on March 1-4, 1972,

at The Americana Hotel, Miami Beach, Florida. Direct all inquiries to; IV Medical/Legal Institute, University of Miami Law Center, P. O. Box 8087, Coral Gables, Florida 33124.

The Student American Medical Association (SAMA) will hold the 22nd Annual Meeting of its House of Delegates at the Biltmore Hotel in Los Angeles, California, beginning Friday, April 28th and continuing through Monday, May 1, 1972. The meeting to elect national officers and Board of Trustees will include exhibits of a health oriented nature. For information contact: Robert L. Jonsson, Student American Medical Association, 1400 Hicks Road, Rolling Meadows, Illinois 60008.

The American College of Physicians will hold its Fifty-Third Annual Session at Atlantic City, New Jersey — April 17-21, 1972. Meetings and Registration - Atlantic City Convention Hall; Headquarters - Chalfonte-Haddon Hall.

The Sixteenth Annual Meeting of the American Society of Internal Medicine is scheduled for April 14-16, 1972, in Atlantic City. For information write to Mr. William R. Ramsey, Executive Director, American Society of Internal Medicine, 525 The Hearst Building, Third at Market, San Francisco, California 94103.

Lon Barton Associates announces availability of many physician applicants who will be separating from military duty next year, and would like to make their availability known to the clinics, groups, medical corporations and hospitals in Puerto Rico. Anyone interested contact Gerald D. Hartman, Director, Physician Staffing Division — Lon Barton Associates, 3325 Wilshire Blvd., Los Angeles, California 90010.

News Release from the Smith Kline & French Laboratories:

The first simple, self-contained test physicians can use in their office to screen for gonorrhea has been developed by Smith Kline & French Laboratories.

The new test's simplicity and convenience permit routine, wide screening for gonorrhea, which is now being recommended by public health officials because of the severity of the problem nationally.

Gonorrhea is now "epidemic", according to the Venereal Disease Branch, Center for Disease Control (CDC), of the U. S. Public Health Service. It is by far the most common reportable communicable disease and its incidence is increasing rapidly. While more than 600,000 cases were reported in the 12-month period ended June 30, 1971, the CDC estimates that the actual number of cases treated annually exceeds two and one-quarter million.

The importance of routine, in-office diagnosis and treatment of gonorrhea is supported by statistics reported in the American Medical Association's *Statement on Venereal Diseases*: that 80 percent of cases are diagnosed by private practitioners.

Routine testing for gonorrhea is especially significant for females. Because the overwhelming majority of infected females (80 to 90 percent) experience slight or no early symptoms, it is difficult for physicians to diagnose the condition without specifically testing for it. Diagnosis is vitally important to stopping the spread of gonorrhea, for until it is made — and treatment carried out — the infected female remains a hidden carrier of the disease.

From the Washington Office - American Medical Association:

President Nixon said his Administration will expand its programs to improve the nation's emergency medical services and to combat diseases of the heart, blood vessels and lungs.

In the long version of his two State of the Union messages to Congress, the President said the "staggering" U. S. death toll from accidents — more than 115,000 last year — "could be greatly reduced by upgrading our emergency medical services." He said it could be done without new scientific breakthroughs if present knowledge were applied more effectively.

From the American Cancer Society, Eleanor Roosevelt International Cancer Fellowships:

The International Union Against Cancer, with the funds provided by the American Cancer Society, will award fellowships for research on cancer.

The awards will be granted to experienced investigators who have demonstrated their ability for independent research and who wish to broaden their experience by a period of study at a single institution in another country.

Fellowships will be granted only to persons on the staff of universities, teaching hospitals, research laboratories or similar institutions.

Fellowships will not be granted to persons who wish primarily to perfect their training in methods of cancer detection or in therapeutic techniques, or who wish to visit briefly several

institutions abroad. The duration of the fellowships ordinarily will be one year but this period may be longer or shorter in special circumstances.

The stipend will be based on the current salary of the applicant and the salary of persons of comparable qualifications in the place where the applicant expects to study.

Applications must be received before 1 September 1972; fellowships being within the twelve months' period following 1 March 1973. For additional information: International Union Against Cancer, P. O. Box 400, 1211 Geneva 2, Switzerland.

Sterling Drug Inc. Statement on PhisoHex:

The proposal of the Food and Drug Administration to place pHisoHex on a prescription basis is, we believe, both premature and illogical. We do not think that the action can be justified on grounds of either safety or science. Further, the action anticipates a study to be carried out by FDA's own panel of experts, and appears to us to be an instance of pre-judgment.

The FDA has based its decision on inconclusive and incomplete animal studies, the results of which we believe cannot be automatically translated to human experience.

Against these small and inconclusive experiments, there stands the unparalleled record of safety and effectiveness of pHisoHex in human use over the past 22 years. Since its introduction in 1949, pHisoHex has been used hundreds of millions of times by members of the health profession and by consumers. In all this massive experience, there has not been a single reported case of neurotoxicity due to pHisoHex when used as directed.

More specifically, in carefully controlled studies — published in the scientific literature and covering more than 102,000 infants in 72 hospital nurseries — there were only 11 reported instances of side effects, all of which were skin irritations.

Prior to the introduction of pHisoHex and similar products into routine hospital usage there were thousands of cases of staphylococcal infections each year among babies in nurseries and among hospital nurses. Many of these infections resulted in death. Over the years, the use of pHisoHex and similar products, coupled with careful procedures, reduced the incidence of severe staphylococcal outbreaks literally to zero.

Significantly, we have been informed that epidemics of staphylococcal infections have broken out in the nurseries of four hospitals which discontinued the use of pHisoHex subsequent to issuance of the FDA Bulletin on Hexachlorophene, dated December 9, 1971. The inference to be drawn is obvious.

The FDA action, in our opinion, appears illogical. The safety of pHisoHex will not be increased by requiring a prescription for its purchase. All that will be accomplished is to lessen its proper use and increase the possibility of serious infection.

What effect will the FDA action have on doctors and the public?

First, by requiring consumers to obtain a prescription to buy pHisoHex, the FDA is placing an additional burden

on the nation's overworked physicians.

Secondly, unless they bear the added cost and inconvenience of obtaining a prescription, millions of Americans will have to cease using this safe and effective antibacterial skin cleanser.

Mothers who wash their hands with pHisoHex before handling their babies, practical nurses and others who use pHisoHex in the sick room, will be deprived of the product's germ-killing effectiveness. For the general public, the danger of hand-borne contamination of food will be increased, since restaurant

workers, butchers, cannery workers and other food handlers who customarily utilize pHisoHex may no longer have it readily available.

Thus the net result of the FDA proposed action may be a widespread increase in serious and perhaps fatal infections, an additional burden on the nation's doctors, an increased cost and inconvenience to the public — all without equivalent benefit to anyone.

Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito: El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos a maquina a doble espacio y por un solo lado de cada página, en duplicado y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor (es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura: Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas: Las tablas deben aparecer en hojas separadas. Estas deben incluir el título y el número de la tabla (romano). Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla.

Figuras: Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor y debe indicarse la parte superior.

Referencias: Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Estas deben seguir el estilo o patrón del "Index Medicus", el cual se describe a continuación:

Para artículos de Revista

Apellido (s), e iniciales del nombre del autor (es), título del artículo, nombre de la revista, volumen, primera página y año.

Koppisch, E.: Pathology of arteriosclerosis. Bol. Asoc. Méd. P. Rico 46: 505, 1954.

Para citación de Libros

Apellido (s), e iniciales del autor (es), título, edición, casa editora, ciudad, año y página.

Wintrobe, M. M.: Clinical Hematology, 3rd Ed. Lea and Febiger, Philadelphia, 1952 p. 67.

Deben usarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana.

Como guía de referencia para preparar su artículo puede usar la publicación Advice to Authors

que publica la Scientific Publications Division, American Medical Association, 535 N Dearborn Street, Chicago, Illinois, 60610.

Instructions to Authors

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts: The entire manuscript, including legends and references should be typewritten double spaced in duplicate with ample margins. A separate title page should include the following: title, authors and their degrees (e. g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgment of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature: Generic names of drugs should be used; trade names may also be given in parenthesis,

if desired. Metric units of measurements should be used preferentially.

Tables: These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted.

Figures: Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

References: These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text. This list should conform to the Style of the Index Medicus and should be punctuated as in the following examples.

For journal articles: Surname and initials of author (s), title of articles, name of journal, volume, first page and year.

Koppisch, E.: Pathology of arteriosclerosis. Bol. Asoc. Méd. P. Rico 46: 505, 1954.

For Books: Surname and initials of author (s), title, edition, publishing house, City, year and page.

Wintrobe, M. M.: Clinical Hematology, 3rd. Ed. Lea and Febiger, Philadelphia, 1952, p. 67.

Abbreviations will conform to those used in the Cumulative Index Medicus, published by the American Medical Association.

For aid in preparing your manuscript refer to the publication Advice to Authors available from the Scientific Publications Division, American Medical Association, 535 N Dearborn St., Chicago, Illinois 60610.

A gratifying announcement about Empirin[®] Compound with Codeine



You may now specify up to five refills within six months when you prescribe Empirin Compound with Codeine (unless restricted by state law).

It is significant in this era of increased regulation, that Empirin Compound with Codeine has been placed in a less restrictive category. You may now wish to consider Empirin with Codeine even more frequently for its predictable analgesia in acute or protracted pain of moderate to severe intensity.

Empirin Compound with Codeine No. 3 contains codeine phosphate* (32.4 mg.) gr. 1/2. No. 4 contains codeine phosphate* (64.8 mg.) gr. 1. *(Warning—may be habit-forming.) Each tablet also contains: aspirin gr. 3 1/2, phenacetin gr. 2 1/2, caffeine gr. 1/2.

Call it what you will, it may be premalignant

Before

3/29/67 Before therapy with 5%-FU cream. Patient P. T. shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

After

6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.





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and Efudex® (fluorouracil) 5% cream can resolve it.

Call it actinic, solar or senile keratoses, many regard it as "precancerous."^{1,2}

Topical fluorouracil, considered by some dermatologists to be a major advance in the treatment of multiple solar keratoses,^{3,4} offers the physician a relatively inexpensive alternative to cryosurgery, electrodesiccation and cold knife surgery. Of the topical fluorouracils available, only Efudex offers 2% and 5% solution and 5% cream formulations—formulations that have proved effective in the treatment of these multiple lesions.

Usual duration of therapy, 2 to 4 weeks.

Studies showed that with the 2% and 5% Efudex preparations, the usual duration of therapy was only 2 to 4 weeks.⁵ Other studies with topical fluorouracil revealed that when concentrations of less than 2% were used, significant numbers of lesions recurred.⁶

Treats the lesions you can't see, too.

Numerous lesions, not apparent prior to 2% and 5% Efudex therapy, manifested themselves by definite reactions, while intervening skin remained relatively unaffected.⁵ The early eradication of these subclinical lesions (which may otherwise have undergone further progression) probably accounts for the reduced incidence of future solar keratoses in patients treated with topical fluorouracil—especially with 5% concentrations.⁶

How to identify solar keratoses.

Typically, the lesion—a flat or slightly elevated brown to red-brown papule—is dry, rough, adherent and sharply defined. Multiple lesions are the rule.

Predictable therapeutic response.

The response to a typical course of Efudex therapy is usually characteristic and predictable. After 3 or 4 days of treatment, erythema begins to appear in the area of keratoses. This is followed by a moderate to intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of this response generally occurs two weeks after the start of therapy and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. Lesions that do not respond should be biopsied.

References: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York, Grune & Stratton, 1967, p. 842. 2. Dillaha, C. J.; Jansen, G. T. and Honeycutt, W. M.: "Treatment of Actinic Keratoses with Topical Fluorouracil," in Waisman, M. (ed.): *Pharmaceutical Therapeutics in Dermatology*, Springfield, Ill., Charles C Thomas, 1968, p. 92. 3. Belisario, J. C.: *Cutis*, 6:293, 1970. 4. Sams, W. M.: *Arch. Derm.*, 97:14, 1968. 5. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and Klein, E.: *Cancer*, 25:450, 1970.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

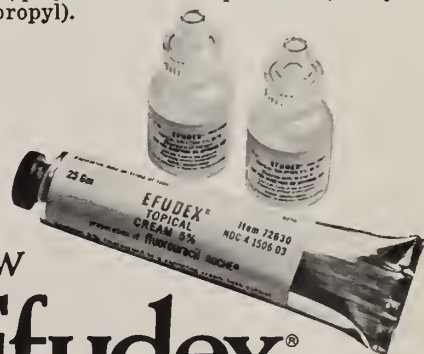
Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

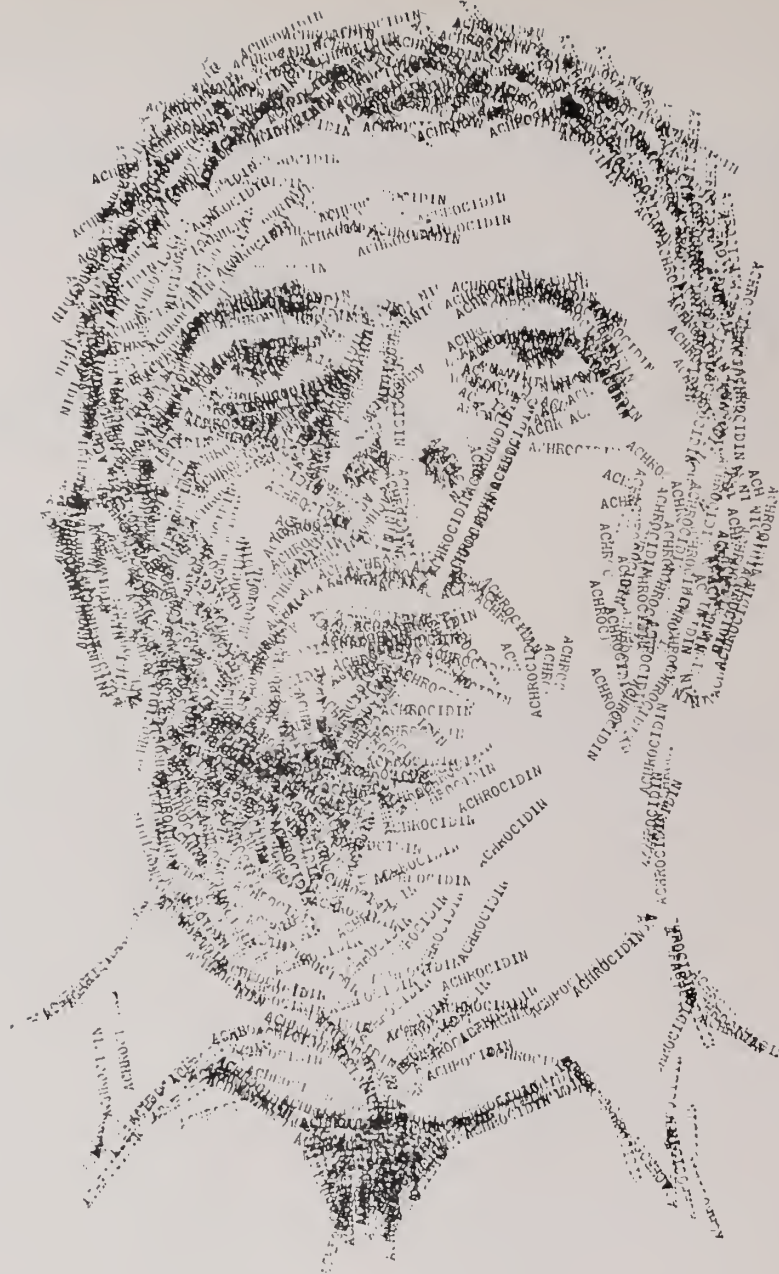
Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



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Efudex®
(fluorouracil)
cream/solution



Achrocidin® Tablets and Syrup

Tetracycline HCl—Antihistamine—Analgesic Compound

Each tablet contains: ACHROMYCIN® Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Caffeine 30 mg.; Salicylamide 150 mg.; Chlorothen Citrate 25 mg.

ACHROCIDIN Tetracycline HCl—Antihistamine—Analgesic Compound Tablets and Syrup are recommended for the treatment of tetracycline-sensitive bacterial infection which may complicate vasomotor rhinitis, sinusitis and other allergic diseases of the upper respiratory tract, and for the concomitant symptomatic relief of headache and nasal congestion. For children and elderly patients you may prefer caffeine-free **ACHROCIDIN Syrup**. Each 5 cc contains: **ACHROMYCIN** Tetracycline equivalent to Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Salicylamide 150 mg.; Ascorbic Acid (C) 25 mg.; Pyrilamine Maleate 15 mg.

Contraindications: Hypersensitivity to any component.

Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.

Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons

on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculo-

popular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

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y no lo que deben...



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10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
Vitamina D	10 mcg.
Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

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anxiety: a time bomb

Unless "defused," anxiety may build up to an intensity that can overwhelm the patient's inner defenses. Also, in one weakened by chronic illness or surgery, excessive anxiety may provoke or aggravate symptoms and interfere with recovery.

The antianxiety action of Librium (chlordiazepoxide HCl)—used adjunctive or alone—has demonstrated clinical usefulness in many fields of medical practice where anxiety complicates the patient's condition.



Librium® (chlordiazepoxide HCl) 5-mg, 10-mg, 25-mg capsules up to 100 mg daily for severe anxiety

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating mo-

chinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending

depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances, syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG pattern (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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NUEVA OPERACION PARA ATRESIA TRICUSPIDEA, PULMONAR Y CONDICIONES
ASOCIADAS CON MALFORMACION DEL VENTRICULO DERECHO 44

I. Aspectos Quirúrgicos

Jorge O. Just Viera, MD, Ernesto Rivé Mora, MD y Olga Rodríguez, MD

IMMUNOSUPPRESSIVE THERAPY – BASIC CONCEPTS AND RECENT ADVANCES 48

Julio E. Lergier, MD

HUMAN MACELLARIA MYIASIS IN PUERTO RICO 53

Irving Fox, MD and Rodolfo Rodríguez Torréns, MD

EMERGENCY MYOCARDIAL REVASCULARIZATION IN PREINFARCTION ANGINA 56

George G. Rowe, MD, George M. Kroncke, MD and William P. Young, MD

DESIGN FOR OLD LIVING. ADVICE ON HOW TO BETTER WITH IT. ... 61

Rafael Rodríguez Molina, MD, FACP

EDITORIAL 62

Current Trends in Cataract Extractions



The negative power of undue anxiety
in congestive heart failure...

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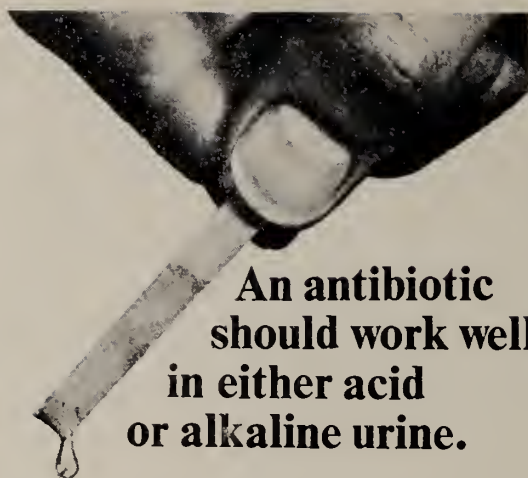
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NUEVA OPERACION PARA ATRESIA TRICUSPIDEA, PULMONAR Y CONDICIONES ASOCIADAS CON MALFORMACION DEL VENTRICULO DERECHO:

I. Aspectos Quirúrgicos

Jorge O. Just Viera, MD
Ernesto Rivé Mora, MD
Olga Rodríguez, MD

Hasta ahora, para el tratamiento de atresia de la tricúspide, atresia pulmonar e hipoplasia del ventrículo derecho, sea en forma aislada o en diferentes combinaciones sólo puede escogerse entre una anastomosis cavopulmonar, una anastomosis entre la arteria pulmonar y la aorta (Waterston) o entre la arteria pulmonar y la subclavia (Blalock-Taussig). La corrección total de estas anomalías no ha sido posible.

Las desventajas de la anastomosis cavopulmonar son bien conocidas desde su aplicación clínica en 1958 por vez primera. Estas son (1, 2):

1. Deja sin oxigenar dos terceras partes del retorno venoso sistémico.

2. Complican la operación con incidencia significativa, trombosis aguda, quilotórax, oclusión tardía de la arteria pulmonar por trombosis o embolia, y disminución tardía del retorno venoso al pulmón derecho.

3. Sus dificultades técnicas añaden peligro al niño enfermo y cianótico.

4. La operación no deja de ser de índole paliativa y puede interferir luego con cualquier intento de corrección total.

Las complicaciones a largo plazo de anastomosis sistémicopulmonares son bien conocidas, primordial entre ellas es el desarrollo de hipertensión pulmonar (3).

Conscientes de estos factores, hemos diseñado un método alterno experimental propio para la corrección total de estas lesiones y deseamos informarlo (Fig. 1). Al interponer un homoinjerto de arteria pulmonar entre el atrio derecho y la arteria pulmonar se logró desviar por completo el retorno venoso sin necesidad de que éste pase por el ventrículo derecho. Logramos así probar también que el ventrículo derecho no es esencial para la hemodinámica del lado derecho del corazón en presencia de pulmones normales y atrio y ventrículo izquierdo intactos.

De la Sección de Cirugía Torácica, Hospital Municipal de San Juan y la Escuela de Medicina de la Universidad de Puerto Rico. Apoyado por la Asociación Puertorriqueña del Corazón y por la Asociación Puertorriqueña para Investigación Médica (APPIM, Inc.).

Materiales y Métodos

Se obtuvo un homoinjerto pulmonar de un perro donante de aproximadamente el mismo peso que el recipiente, el mismo día de la operación. Al disecar la arteria pulmonar se protegió la válvula pulmonar cuidadosamente. Después de anestesiado el recipiente con barbitúricos, se abordó a través del hemitórax derecho. Con ayuda de una pinza vascular, la arteria pulmonar del recipiente fue ocluída parcialmente y se unió la arteria pulmonar del donante a la arteria pulmonar del

recipiente en una anastomosis término lateral con seda 000000. Amputada la orejuela derecha, ocluída su base por la misma pinza vascular, la pared atrial se unió al anillo de la válvula pulmonar injertada con sutura plástica 00000, con atención especial para preservar al máximo el volumen atrial. Después de construido el puente atriopulmonar, y tras incluir oclusión venosa total, se exploró el atrio derecho. Una vez localizada la válvula tricuspídea, ésta se cerró por completo con seda 00.

En otro grupo de animales, intentamos aumentar el volumen del atrio por medio de un delantal de pericardio obtenido del recipiente y suturado en la base de la arteria pulmonar injertada. De esta forma, las líneas de sutura del atrio derecho quedaron a niveles distintos, lo cual creímos conveniente para evitar trombosis. La válvula tricuspídea se cerró como ya hemos descrito.

En un tercer grupo procedimos a simular estenosis de la válvula tricuspídea, al cerrar la mitad del orificio de la válvula. Simultáneamente se abrió una comunicación interatrial para descomprimir el atrio derecho, según el método descrito por Warden y sus colegas (4), el cual de por sí lleva una mortalidad operatoria alta. Recuperados de esta intervención, los sobrevivientes fueron abordados por una nueva toracotomía para interponer el homoinjerto, como se explica anteriormente, y la válvula tricuspídea fue cerrada por completo sin intentar ocluir el defecto interatrial. No se usó circulación extracorpórea.

De tiempo en tiempo, el uso de angiocardiografía permitió el estudio de los sobrevivientes a largo plazo. También se obtuvieron en ellos medidas de la presión venosa central, presión arterial, gases sanguíneos y estudios de presiones intracardíacas por medio de sondeo cardíaco. Los resultados de estos estudios serán informados con más detalle luego.

Resultados

Los resultados obtenidos en el primer grupo de animales revelaron dos sobrevivientes a largo plazo de 6 animales operados. Las causas de muerte fueron derrame pleural, atelectasia masiva y trombosis del injerto secundario a la presencia de gusanos intracardíacos. Todas es

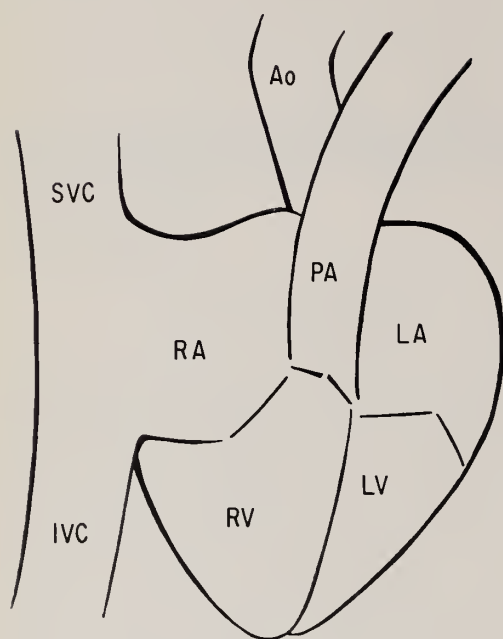
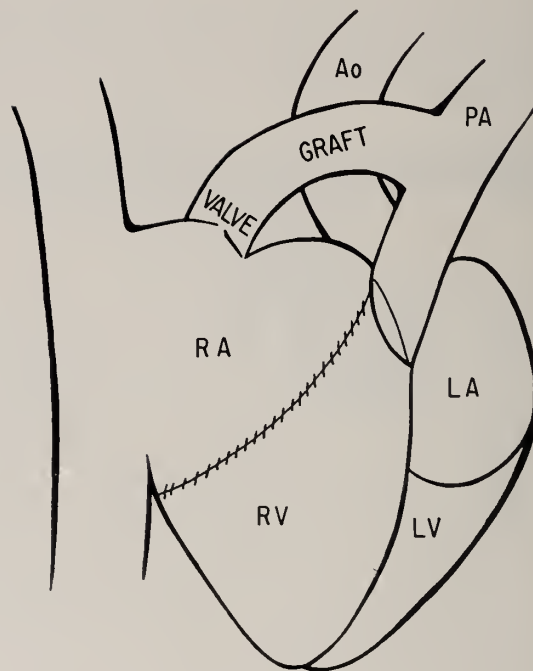
**NORMAL****POST OPERATIVE**

Fig. 1: Muestra los aspectos quirúrgicos de la operación ensayada experimentalmente para corrección total de atresia de las válvulas tricúspide y pulmonar, ventrículo único y condiciones asociadas con malformación del ventrículo derecho. En el diagrama postoperatorio la válvula tricúspídea fue cerrada quirúrgicamente y se interpuso un homoinjerto, de arteria pulmonar con su válvula entre la orejuela derecha y la arteria pulmonar del recipiente. (Reimpreso del Surgical Forum, Vol. XXII: 166, 1971, con permiso del American College of Surgeons.)

tas complicaciones disminuyen la velocidad del torrente sanguíneo y llevan a trombosis. Dos animales han sobrevivido ya 16 meses y continúan saludables y activos, sin signos de edema sistémico o cerebral. No están limitados su actividad ni su ejercicio y tampoco hay indicios de rechazo del injerto a pesar de que no reciben esteroides o inmunosupresivos.

En el segundo grupo de animales, cuando se ensayó aumentar el volumen atrial con pericardio, 4 de 10 animales no sobrevivieron el período postoperatorio inmediato. Tres sucumbieron de hemorragia y uno murió súbitamente sin que lográramos explicar la causa. Otro animal murió a las tres horas del acto operatorio debido a una reacción transfusional, y la autopsia demostró el homoinjerto completamente abierto. Un animal murió 18 horas después de operado debido a apnea irreversible tras administrarle un relajante muscular. Este fue el

único animal en que se intentó terapia respiratoria a largo plazo para evitar atelectasia. Por presentar problemas respiratorios, se sacrificó un animal a las 24 horas y encontramos trombosis del homoinjerto, resultado de un error técnico en la construcción del delantal pericárdico. Otro animal sobrevivió cuatro días, cuando fue sacrificado por encontrarse en dificultades cardiopulmonares. Se encontró una sutura suelta con insuficiencia de la válvula tricúspídea, y, además, bloqueo completo del corazón. El injerto estaba patente. Un animal fue sacrificado 15 días después de operado y se encontró trombosis parcial del homoinjerto por abundante cantidad de gusanos intracardiácos. El último animal sobrevivió 5 meses, y falleció un mes después de catesterismo cardíaco. En retrospecto, las radiografías tomadas durante el cateterismo demostraron el paso forzado de una sonda hasta el ventrículo derecho a través de la

válvula tricuspídea. Aparentemente, al restablecerse el flujo sanguíneo por la arteria pulmonar del recipiente, disminuyó el flujo en el injerto, y éste se ocluyó como consecuencia.

De diez animales en el tercer grupo sometidos inicialmente a estenosis parcial de la válvula tricúspide, sólo tres sobrevivieron la primera etapa. Estos pasaron por la segunda etapa, interposición del injerto y cierre de la válvula tricuspídea. Un animal murió 48 horas después de la operación con hemotórax y embolia pulmonar, oriunda en el ventrículo derecho. El defecto interatrial había cerrado y el homoinjerto continuaba abierto. Un animal murió 5 días después de la operación. La autopsia demostró oclusión parcial del homoinjerto (80 por ciento) y empiema. El defecto interatrial y la válvula tricuspídea estaban abiertos. Un animal sobrevivió más de siete meses, cuando fue sacrificado después de un episodio clínico de descompensación cardíaca. La autopsia reveló oclusión tardía del injerto.

Discusión

Indudablemente, el tratamiento ideal de anomalías cardíacas estriba en su corrección total y el establecimiento de una homodinámica normal. Hasta ahora, ha sido imposible lograr esto en caso de anomalías severas como atresia de las válvulas tricuspídea y pulmonar, hipoplasia, o atresia del ventrículo derecho, y ventrículo único.

Una anastomosis cavopulmonar podrá mejorar inicialmente la decompensación cardíaca en estas anomalías, al disminuir el retorno venoso, pero conlleva una alta incidencia de trombosis. En cambio, las anastomosis sistémico-pulmonares aumentan la posibilidad de decompensación cardíaca inmediata, y además, ocasionan aumento del gasto cardíaco, mayor dificultad para el ventrículo derecho en expulsar sangre hacia el pulmón, y suplen sangre que no es venosa (3). La operación ideal sería la que devolviera toda la sangre venosa al pulmón para oxigenación. Esto ha sido posible con un puente atriopulmonar mediante injerto de arteria con válvula pulmonar, según hemos demostrado.

Nuestros experimentos tienen base sólida en trabajos anteriores que dejaron establecida la posibilidad de excluir al ventrículo derecho de la circulación. Tanto Starr y su grupo (5), además de Kagan (6), y Bakos (7), demostraron el grado de daño que puede afectar al ventrículo derecho sin alterar significativamente la hemodinámica. Robicsek y su grupo (8) excluyeron al ventrículo derecho totalmente excepto por el retorno sanguíneo a través del seno coronario. Intervinieron

quirúrgicamente por etapas; la cava superior fue conectada primero a la arteria pulmonar derecha, y luego, la cava inferior al atrio izquierdo. Cuatro años después la presión en la cava superior era de 13/10 mm Hg, y la saturación arterial de oxígeno 80 por ciento.

Anteriormente la orejuela había sido conectada directamente a la arteria pulmonar (4, 9). Por no existir una válvula entre el atrio derecho y la arteria pulmonar, esta operación funcionó como insuficiencia tricuspídea, al impulsar el ventrículo derecho sangre a través de la anastomosis, hacia el atrio derecho, situación obviada en nuestro experimento por la válvula pulmonar del donante. Se dejó establecido, además, que la fuerza de contracción del atrio derecho es suficiente para propulsar sangre a través del desvío a la arteria pulmonar, si no existe hipertensión pulmonar. Por lo bien que es conocida la propensión a trombosis y estrechez de las anastomosis del atrio, creímos conveniente añadir el delantal de pericardio mencionado para evitar que las líneas de suturas estuviesen superimpuestas. Esto sería innecesario en la atresia tricuspídea, pues en esta condición el atrio es grande. Por otro lado, ya es aceptado el uso de homoinjertos para tratamiento de tronco arterioso, tetralogía severa y atresia pulmonar donde exista un buen ventrículo derecho.

En resumen, ¿cuáles son las ventajas de esta nueva operación? Primero, se devuelve todo el retorno venoso al pulmón para oxigenarse, y esto resulta en una saturación arterial normal. Segundo, disminuirán las complicaciones importantes como trombosis (el flujo sanguíneo a través de la anastomosis es mayor) y quilotórax, porque la disección quirúrgica es limitada y la presión venosa central final es baja. Tercero, la fuerza propulsiva del atrio derecho hipertrofiado posiblemente permitirá el tratamiento de algunos niños con un leve aumento en presión pulmonar. Cuarto, al cerrarse la comunicación interatrial existente, se disminuirá el trabajo del lado izquierdo del corazón. Quinto, la presencia de una válvula entre la circulación pulmonar y la venosa protege del establecimiento de un corto circuito sanguíneo.

Para nosotros constituye lo más cercano posible a una corrección fisiológica total.

Entre los factores desconocidos de esta nueva operación, está el resultado a largo plazo de homoinjertos en niños y si luego compensará durante el crecimiento.

Los resultados experimentales, sin embargo, apoyan aplicación clínica cautelosa. En este caso recomendaríamos el uso simultáneo de un parcho perforado para cerrar el defecto interauricular lentamente y permitir la decompresión del atrio derecho durante el período

operatorio inmediato. Desafortunadamente, por razones ajenas a nuestra voluntad, no hemos podido llevar a cabo aún la intervención quirúrgica en humanos.

Resumen

Se ha ensayado experimentalmente una nueva operación diseñada para lograr corrección total fisiológica para atresia tricuspídea, pulmonar y condiciones asociadas con malformación del ventrículo derecho. Después de simular atresia tricuspídea al suturar la válvula tricuspídea, se interpuso un homoinjerto de arteria pulmonar, con su válvula, entre el atrio derecho y la arteria pulmonar del recipiente. Se obtuvieron 4 sobrevivientes a largo plazo. Causas de trombosis del desvío fueron las asociadas con disminución en flujo sanguíneo: atelectasia, hemo o hidrotórax y gusanos intracardíacos.

Los resultados obtenidos apoyan la aplicación clínica cautelosa de esta operación en atresia de las válvulas tricuspídea y pulmonar, atresia o hipoplasia del ventrículo derecho, y, también, en ventrículo único.

Summary

A new operation, intended for total physiologic correction of tricuspid and pulmonary valvular atresia, as well as malformation of the right ventricle has been evaluated experimentally. After simulating tricuspid atresia by suturing shut the tricuspid valve, a pulmonary valve and artery homograft was placed between the right atrium and the recipient pulmonary artery. Four long term survivors were obtained. Causes of shunt failure resulted in diminished blood flow: these were atelectasis, hemothorax or effusion, and intracardiac worms.

Results obtained support cautious clinical application of this operation in tricuspid valve atresia, pulmonary valve atresia, hypoplasia or atresia of the right

ventricle, and single ventricle.

Reconocimiento

Deseamos reconocer la valiosa ayuda del personal del Laboratorio de Cirugía Experimental de la Escuela de Medicina de la Universidad de Puerto Rico.

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IMMUNOSUPPRESSIVE THERAPY — BASIC CONCEPTS AND RECENT ADVANCES

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During the past several years the developments in the field of immunosuppressive therapy — the therapeutic repression of undesired immunologic mechanisms — have been many, as has been the interest in this area of medicine, which is evident in the numerous reviews which have been published (1-6, 8-13). It is the purpose of this article to summarize the more important aspects of immunosuppression and point out some recent contributions in the English literature.

General Concepts

One of the major problems in the clinical application of immunosuppression has been the lack of specificity or the “generalized” type of suppression which precludes the selective control of certain unwanted immune mechanisms (1), while at the same time resulting in undesirable side effects and complications (14).

There is a marked variability of the type and degree of immunosuppressive effect, depending on the various agents (2), doses (3), timing (4), species (5), and vehicle of administration (15). Through manipulation of different agents in variable doses it has been possible to dissociate cellular from humoral immune responses and IgG from IgM immunoglobulin responses to antigenic stimulation (6, 16).

The design of immunosuppressive regimes is based on an understanding of the mechanisms of immune responses — both normal and pathogenetic, and it has been suggested that major control of diseases mediated by common immune injury patterns can only come from a better knowledge of the primary etiologic factors, which usually are unknown (6).

Immunosuppressants: Sites of Action

One may look at the site of action of immunosuppressants in terms of general immunologic mechanisms of response or in terms of molecular effects.

It must be stressed that most agents may have not a single but multiple mechanisms of action, both immunologic, or non-immunologic. Non-immunologic mechanisms include non-specific anti-inflammatory effects mediated through damage to bone marrow precursors of cells such as macrophages and granulocytes (14) or through functional impairment of specific components of an inflammatory response, such as stabilization of lysosomal membranes (17). The possible role of antiviral effects, which have been demonstrated for some agents such as cytosine arabinoside, remains to be established (18).

(A) General Immunologic Scheme:

Modern concepts of the immune response are based on a theory of a dual component immune system with cellular and humoral components arising from common lymphoid marrow precursors which “differentiate” under the action of the thymus or of “bursal equivalents” to yield respectively T-lymphocytes, responsible for cellular immunity or B-lymphocytes, responsible for humoral immunity (see Figure 1).

Excellent reviews by Schwartz (1), Finkelstein (8) and Berenbaum (9), point out that both humoral and cellular primary immune responses consist of three stages (Figure 2):

(1) Induction stage — Antigen, probably after “processing” of the antigen by macrophage acts on antigen sensitive, uncommitted cells. These are undifferentiated cells which are not committed to the production of specific antibody or cellular mediators.

(2) Proliferative stage (post antigenic challenge) — Sensitized, now committed cells proliferate, with synthesis of DNA, RNA and protein, mitosis and differentiation which results in the production of humoral and cellular “effector” mediators, which are described below.

(3) Effector stage:

(a) Humoral mechanisms consist of the production of antibody by plasma cells derived from the “B-lymphocytes” after appropriate antigenic stimulation and participating in immune injury in a number of ways: immune complex (antigen-antibody) disease, anaphylaxis, cytolysis, agglutination and inactivation.

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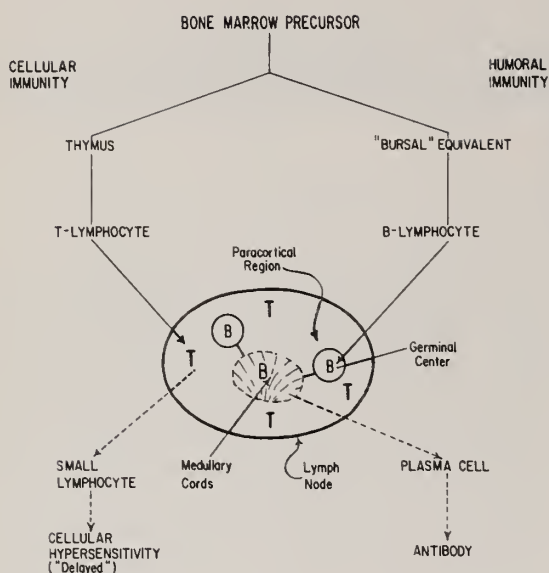


Fig. 1: Dual component theory of the immune response.

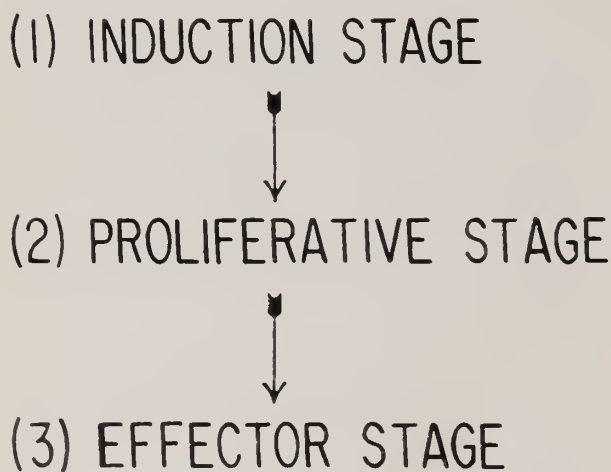


Fig. 2: Three stages of the immune response.

The ultimate injury may be mediated by complement components, lysosomal enzymes derived from polymorphonuclears, "chemical inactivation" (ex: circulating anticoagulants), chemical mediators (histamine, bradykinin, slow-reactive substance, serotonin) or by reticuloendothelial system damage (macrophagocytosis).

(b) Cellular mechanisms consist of the liberation by committed "T-lymphocytes" upon antigenic stimulation of effector molecules such as lympho-

toxin and macrophage migration inhibitory factor (MIF) which "recruits" macrophages to participate in the cellular immune process directly and via lysosomal enzymes and transfer factor (TF) which transfer to other non-committed lymphocytes the ability to respond to the specific antigen. All these factors result in what is termed "delayed hypersensitivity".

The agents acting at the "induction stage" include steroids, radiation, antibody and antilymphocyte serum (ALS). At the "proliferative" stage the most important agents are the cytotoxic drugs, although steroids, radiation, antibody and ALS may also act at this stage. Finally, effector mechanisms may be "broken" by steroids (lysosomes), radiation (macrophages), antibody (blocking or enhancing antibody) and cytotoxic drugs (macrophage and leukocyte precursor damage). In effect, this final anti-effector mechanism may be very important in as yet not clearly defined terms, as some studies have failed to show a definite correlation between the degree of immunologic "suppression" and the clinical improvement in the conditions treated (19).

(B) Molecular Effects:

These are based on an understanding of the concept that biologic responses of cells are mediated by the sequence: DNA → RNA → Protein synthesis → effect. The specific molecular sites of action of various cytotoxic agents and hormones have been reviewed by Berenbaum (9), Dollinger *et al* (20), and Kline (21), and are as follows:

(1) Anti-DNA agents: radiation and mitomycin (chain split); alkylating agents and mitomycin (cross-linking); procarbazine (depolymerizes); antimetabolites: antipurines, antypyrimidines, antifolic acid agents (decrease synthesis and produce abnormal "base" substitutions); actinomycin (complexes with DNA blocking RNA polymerase).

(2) Anti-RNA agents: chloramphenicol, thiophamphenicol (block the attachment of messenger-RNA to ribosomes); steroids (? mechanism).

(3) Anti-protein (polypeptide) synthesis agents: DON, azaserine (glutamine inhibitors): L-asparaginase and L-glutaminase (increase destruction of specific aminoacids); steroids (? mechanism).

(4) Anti-mitotic spindle agents: Vinea alkaloids, colchicine.

Again it is noted that agents may act at more than one molecular site, as any agent acting on DNA or RNA synthesis may impair mechanisms mediated by protein "effector" molecules (polypeptides) whose synthesis is impaired.

Immunosuppressants: Specific Agents

Clinically tried or potentially useful agents include: radiation (22, 23), steroids (24, 25), antilymphocyte serum (26, 27), cytotoxic drugs: 6-mercaptopurine (28), azathioprine (19, 29), methotrexate (19, 30), cyclophosphamide (4, 31, 32), actinomycin D (33), and some recently studied agents such as: 5-Fluorouracil (16), cytosine arabinoside (30), L-asparaginase (34, 35), L-glutaminase (36), thioamphenicol (37), perhaps alpha-adrenergic blocking agents (38), and antibody (39). Long-term immunosuppressive effects of combination chemotherapy for acute leukemia are being studied (40). Recently different approaches to immunosuppression are being tried. These include induction of tolerance by antigen administration (41, 42), and removal of circulating antigen and/or antibody by extracorporeal passive immunoadsorption in experimental animals (43).

Clinical Aspects of Immunosuppression

(A) Applications:

The uses of immunosuppression in clinical practice are mainly in organ transplantation (44, 45), including the management of "acute" rejection episodes (33, 46), and in the management of "auto-immune" disorders. This latter category includes a heterogeneous and ill-defined group of diseases in which much controversy exists as to the value of immunosuppression. Recent reviews have summarized the status in this area (10, 13). In general, disorders where significant improvement has been noted with the use of immunosuppression include: autoimmune hemolytic anemia-azathioprine (29, 47); chronic idiopathic thrombocytopenic purpura-azathioprine (29, 48); lupus nephritis-azathioprine (37, 49, 50), cyclophosphamide (51), thioamphenicol (37); Wegener's granulomatosis-alkylating agents (52, 54), azathioprine (52, 53), methotrexate (55); regional ileitis-azathioprine (56, 57); rheumatoid arthritis-cyclophosphamide (32), azathioprine (58), and polymyositis-azathioprine (59). Questionable benefit not significantly greater than with steroids alone has been noted in ulcerative colitis (60), and chronic active hepatitis (61, 62). No significant benefit has been noted in scleroderma (63). In chronic proliferative renal diseases, controlled clinical trials have not shown statistically significant improvement after immunosuppressive therapy with azathioprine and steroids (64). These studies did not include patients with lupus nephritis or Wegener's granulomatosis, conditions in

which, as stated before, significant improvement in renal status has been noted after immunosuppressive therapy. Steroid-dependent children with relapsing nephrotic syndrome may constitute another indication for immunosuppressive therapy (65). It should be noted that in most of these disorders, with the possible exception of advanced proliferative lupus nephritis and Wegener's granulomatosis, a trial with steroids is probably warranted prior to the use of more powerful cytotoxic agents. This is more so in view of the possible severe complications of immunosuppression (*vide infra*).

(B) Complications:

(1) Infections are common with life threatening, sometimes opportunistic, mainly obligatory intracellular organisms, including Viruses-Cytomegalovirus; Fungi-Candida albicans, Histoplasmosis, Cryptococcus; Protozoans-Pneumocystis carinii and Bacteria-gram negative bacilli, mycobacteria (14, 66).

(2) Tumor induction in long-term immunosuppressed homograft recipients on azathioprine has been described in over 40 patients (67), and the possible mechanisms involved reviewed (68). These tumors include both epithelial and lymphoid origin tumors. Epithelial tumors have been either superficial and associated with a good prognosis or deep and having a poor prognosis (67). Lymphoid tumors have been characterized by a particularly high incidence of central nervous system involvement and a very aggressive, rapidly fatal course (69). This complication has not yet been described with other immunosuppressants such as cyclophosphamide alone or in non-transplant patients.

(3) Non-specific side effects such as bone marrow depression (pancytopenias), gastrointestinal toxicity (nausea and vomiting), skin and mucosal toxicity (alopecia, ulcerations, hemorrhagic cystitis) may occur, specially at high dosages or in "sensitive" patients.

It has been suggested that immunosuppressive therapy of non-neoplastic diseases with cytotoxic agents be limited to the management of life threatening conditions refractory to therapy with conventional drugs such as steroids (70). More specific guidelines for the use of immunosuppression in clinical practice are being sought from various clinical and experimental studies.

Summary

The field of immunosuppressive therapy has had wide interest and many new developments. This review has presented some recent advances and basic concepts of the sites of action of immunosuppressive agents, both

in terms of the general immunologic response and in molecular terms. The many immunosuppressive agents presently or potentially useful are mentioned and finally the clinical applications of immunosuppressive therapy for organ transplantation and "autoimmune" diseases discussed, with a brief mention of the possible complications of this therapy, such as infections or tumor induction.

Resumen

El campo de la terapia inmunosupresiva ha tenido amplio interés y muchos nuevos acontecimientos. Este repaso de la literatura ha presentado algunos avances recientes y conceptos básicos de los puntos de acción de los agentes inmunosupresivos, en términos de la respuesta inmune en general y en términos moleculares. Los muchos agentes inmunosupresivos al presente o potencialmente útiles han sido mencionados y finalmente se han discutido las aplicaciones clínicas de la terapia inmunosupresiva para el transplante de órganos y las enfermedades "auto-inmunes", con una mención breve de las posibles complicaciones de esta terapia, tales como las infecciones y la inducción de tumores.

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HUMAN MACELLARIA MYIASIS IN PUERTO RICO

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Myiasis is the invasion of living tissues of man and animals by the larvae (or maggots) of various species of flies. Eleven cases of human myiasis have been reported from Puerto Rico, but in only six of them were the maggots recovered and identified (1, 2). In each of these six cases the primary screwworm, *Cochliomyia hominivorax* (Coquerel) caused the myiasis. Our present case is of unusual interest because a different species of fly was involved.

Case Report

An 87-year old man was admitted to the San Juan City Hospital on January 1, 1971 with a long time history of bilateral paresthesia and numbness of both legs which later on turned into intermittent claudication and severe pain not alleviated by rest. He was brought to the emergency room with gangrenous involvement of the left leg. This patient was a prisoner at the State Penitentiary where he had been confined for the last two years prior to admission. Physical examination showed an undernourished negro male in moderately severe pain distress. No arterial pulses were felt in the left leg which showed marked necrotic discoloration, desquamation of the distal part, cold skin, crepitaney, and a foul odor. He was admitted directly to the operating room where an A-K amputation was performed. After operation, he was transferred to the medicine service isolation ward and three days later the gangrenous process was found to be extending upward. Desarticulation of the left hip was considered but not performed because of the patient's poor condition, low haemoglobin, and the unavailability of his blood type for transfusion. Urinary tract infection and sepsis complicated his condition in spite of treatment with antibiotics and polyvalent gas gangrene antitoxin.

Nine days after admission during a morning examination a few maggots were noticed in the perianal region. Rectal examination revealed a bulk of more than 100 maggots which appeared to be actively feeding on tissue. Careful examination of decubitus ulcers failed to show any maggots. It seemed that only the rectal area was involved. Several specimens were collected and sent to a specialist who determined them as the larvae of the secondary screwworm fly, *Cochliomyia macellaria* (Fabricius). No treatment was given for the myiasis. The patient died 15 days after hospitalization.

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Discussion

The secondary screwworm fly, *C. macellaria* is not a true parasite since it usually breeds in decaying organic matter and only occasionally invades living tissues. Widely distributed in North, South, and Central America and the West Indies, the species is common in Puerto Rico. James (3) states that the eggs are deposited in masses ranging from 40 to more than 1,000 and hatch in a few hours into larvae which attain maturity in 6 to 20 days and then leave the breeding medium crawling into the soil to pupate; the total period from egg to adult ranging from nine to 39 days depending on the temperature and humidity. Adults are omnivorous feeding on both plants and animals including carrion, putrefying meat, fruits, and vegetables, and even flower nectar. Larvae breed often in dead animals; they are worm-like, yellowish white in color but sometimes dark because of ingested material (Figure 1), about 13 mm. in length, with the anterior end tapering to a point while the posterior end may be broadly truncate. Like the primary screwworm, *C. hominivorax*, the secondary screwworm has bands of spines which give them the screw-like appearance. Even the pupa, which is brown in color and about eight mm. long (Figure 2), has faint rings of spines. Adults are medium sized, about eight mm. long, and green in color with orange eyes and the thorax has three broad black longitudinal bands dorsally. Figure 2 shows the larva, pupa, and adult and Figure 3 shows adults in different positions; the specimens being from a laboratory colony.

From 1965 to 1969 a colony of *C. macellaria* was maintained in the School of Medicine, San Juan. We obtained specimens originally by exposing a dead rat among the School's garbage cans. Adults were housed in a cage 55 x 50 x 42 cm. and fed on a sugar-milk solution which consisted of four teaspoons of powdered milk and four teaspoons of sugar in 300 ml. water poured over cotton in a Petri dish. Under our laboratory conditions adults lived several weeks and there were about 10 generations a year. The larval rearing medium consisted of one teaspoon of dried

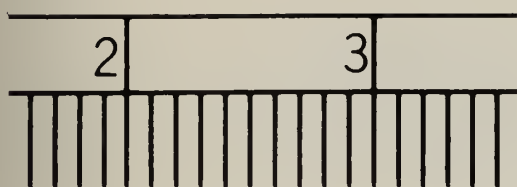


Fig. 1: Larva or maggot of the secondary screwworm fly, *Cochliomyia macellaria* (Fabricius) taken from the patient.



Fig. 2: The larva, the pupa, and the adult of *C. macellaria* from a laboratory colony.



Fig. 3: Specimens from a laboratory colony showing the lateral, ventral, and dorsal aspects of the adult fly (*C. macellaria*).

beef blood, four tablespoons of canned meat cat food, and water to moisten. To obtain larvae a finger bowl containing the larval medium was placed in the cage. After one or two days when egg masses and larvae were seen in the medium, the finger bowl was covered with a cloth and put in a dark place, where in five or six days the larvae became full-grown. For pupation, mature larvae were removed from the larval medium and placed in a large jar with sand on the bottom where they became pupae. Pupae were collected in Petri dishes which were placed in the cage and adults emerged from them in five to seven days.

So great is the interest in myiasis as a medical problem that an abundant literature is recorded. During the first six months of 1971 Index Medicus records 12 papers on the subject and from 1961 to 1971 there were listed 223 articles. Scott (4) analyzed 111 cases of human myiasis which occurred in Canada, Continental United States, Puerto Rico, and Hawaii from 1952 to 1962, and indicated 28 percent of the cases as enteric myiasis but none had been caused by the secondary screwworm. However, *C. macellaria* did cause a case of aural myiasis in Idaho in 1954, and one case of wound myiasis in 1958 in New York (5). Another case of aural myiasis due to *C. macellaria* occurred in 1965 in Georgia (6).

In Puerto Rico various species of flies may be involved in myiasis. Such cases are important not only from the scientific point of view but also because fly larvae feeding on living tissue may cause pain and injury to the patient. In addition to removing all larvae, the physician should preserve some of them in alcohol and send them to an entomologist for identification.

Summary

We report a case of myiasis of the rectum and perianal region in an 87-year old man in Puerto Rico which was due to the secondary screwworm fly, *Cochliomyia macellaria* (Fabricius). The life cycle of the fly and a method for rearing it in the laboratory are given with a review of recent literature on the species as a cause of human myiasis.

Resumen

Se trata de un caso de miasis del recto y la región perianal de un hombre de 87 años de Puerto Rico debido al gusano secundario del ganado, *Cochliomyia macellaria* (Fabricius). El artículo incluye el ciclo de vida de la mosca y un método para criarla en el laboratorio. Se discute además la literatura reciente acerca de la especie como una causa de miasis humana.

Acknowledgments

Thanks are expressed to Dr. Ernesto Marchand and Dr. José Oliver-González for advice and encouragement; to Dr. Robert I. Fox and Dr. Robert P. Belihar for designing methods for rearing flies; to Dr. R. J. Gagne for identifying the larvae taken from the patient; to Dr. M. T. James for identifying the flies from the laboratory colony; to Miss Carmen Romaguera Mollfulleda for making a survey of the literature; and to Mr. José R. Ramírez and Mrs. Ileana G. Bayona for taking the photographs.

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EMERGENCY MYOCARDIAL REVASCULARIZATION IN PREINFARCTION ANGINA

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George M. Kroncke, MD
William P. Young, MD

From large statistical studies it is clear that the life expectancy of subjects with angina pectoris is markedly less than that of normal individuals with mortality approaching 10 percent per year (1, 2). It is possible by selecting those with cardiomegaly (1,3), or electrocardiographic abnormalities such as ST segment deviation or conduction defects (2-5), a positive electrocardiographic exercise tolerance test (6) or abnormal risk factors for atherosclerosis (7-12), to identify groups with an even higher risk rate. Furthermore it is established that approximately 70 percent of patients dying from coronary atherosclerotic heart disease do so before they reach the hospital (13-15). Indeed recent data indicate that death is the first and only symptom in 12 percent of subjects and that 80 percent of those who die from myocardial infarction do so during the first attack (16). These gloomy statistics give us no comfort that the classical methods of treating atherosclerotic coronary artery disease are so successful or sacred that new methods cannot be tried.

It has been stated recently that 65 percent of individuals who have myocardial infarction have symptoms of such nature that they may be recognized in retrospect as a prodrome (17). Although it is not known how many subjects go through such exacerbations of symptoms without developing myocardial infarction, there are a group in whom the symptoms are so severe and incapacitating that hospitalization is requested and obtained. If symptoms do not subside quickly some definite decision concerning therapy must be made. A series of five subjects with such an exacerbation or recent onset of severe anginal pain who have had emergency myocardial revascularization constitute the basis of the present report.

Case Summaries

Case One - R.C. UWH No. 339493

A 39-year old carpenter, whose grandfather died of a myocardial infarct, whose father had several strokes, and whose mother and aunt had angina, had chest pain beginning 10 days prior to hospitalization. The pain was progressively more severe, substernal, oppressive in nature and radiated into both arms. On the evening of admission he had a severe episode of constricting pain lasting 30 to 40 minutes accompanied by profound diaphoresis. He was admitted to the intensive care unit where serum enzyme levels were borderline but not diagnostic of infarction. It was considered that he had severe ischemia but not infarction so coronary arteriograms were done. The left anterior descending and the circumflex coronary artery were moderately diseased but there was a short segment in the right main coronary artery which was severely obstructed (Fig. 1). At operation on 9-10-68 there was no visible evidence of infarction. During an attempt to remove the right coronary arterial plaque a 12 centimeter section of atherosclerotic media and intima easily shelled out of the right coronary artery (Fig. 1B). Postoperatively the patient did well. Repeat coronary arteriography (Fig. 1C) showed wide patency

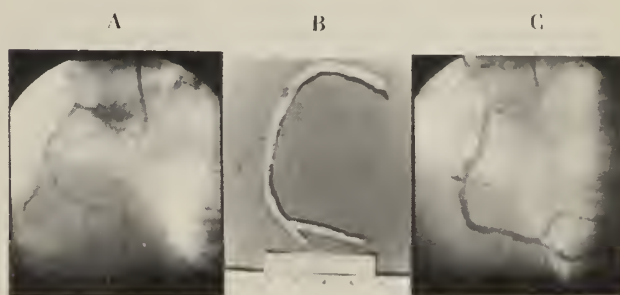


Figure 1 - A is a single frame from a preoperative coronary arteriogram which reveals a severe obstruction in the mid-portion of the right coronary artery. B shows the specimen removed from the right coronary artery at operation. This core shelled out easily from the aortic orifice to the end, representing the posterior interventricular and A-V groove branch of the right coronary artery. C is a single frame from the postoperative coronary arteriogram revealing the patent right coronary artery. The location of the suture line is seen through which the endarterectomy was done.

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of the right coronary artery with minimal narrowing at the suture line where the endarterectomy was done. The patient remains well and at work as a carpenter.

Case Two - J.L. UWH No. 603406

A 39-year old male machinist with progressive exertional chest pain of six weeks duration was transferred from the Intensive Care Unit of an outside hospital to the University Hospital because of marked electrocardiographic changes during pain. When no specific evidence for infarction was found coronary arteriograms were done, which demonstrated marked narrowing of the left main coronary artery at its orifice from the aorta (Fig. 2A). At operation on 7-11-69 the orifice of the left coronary artery was dilated with a series of probes and a saphenous vein graft was placed from the aorta to the left anterior descending coronary artery. Postoperatively coronary arteriograms revealed a widely patent orifice from the aorta and the saphenous vein graft to the left coronary artery (Fig. 2B). The patient continues work and has done well.

Case Three - C.H. UWH No. 385588

A 37-year old male mechanic had had a large interatrial septal defect repaired in 1965. He did well until four weeks prior to admission when he developed exertional dyspnea and sharp nonradiating pain in the left chest, precipitated by exertion, relieved by rest and nitroglycerin but of progressively increasing severity. Three days prior to admission he had much more severe chest pain so when his local doctor expressed concern over his ECG but did nothing more he came to the University Hospital. His initial electrocardiogram in the intensive care unit was abnormal but not diagnostic of infarction and borderline serum enzymes decreased over several years. It was decided that he had had a severe ischemic episode, but not an actual infarction, therefore coronary arteriograms were done which revealed a localized lesion of the left anterior descending coronary artery (Fig. 3A). There was no evidence of collateral from the right coronary artery to the left. Contraction of the anterior wall of the left ventricle appeared to be poor but present. To prevent myocardial infarction a saphenous vein bypass graft was placed from the aorta to the diagonal branch of the left anterior descending coronary artery on 12-8-69. Repeat coronary arteriograms twenty days later, revealed that the graft was patent but the diagonal branch was seriously constricted immediately distal to the entry of the graft (Fig. 3B). Subsequent to the coronary arteriograms he developed a typical myocardial infarction, with an embolus to the aortic bifurcation. The patient has done poorly, is unable to work, and has received treatment for cardiac failure.

Case Four - N.M. UWH No. 054377

N. M., a 60-year old judge, had intermittent chest pain relieved by nitroglycerin over a year and one-half, but without any clear myocardial infarction. One to two months prior to coming to the University Hospital the steady course of his disease was changed by a rapidly progressive increase in severity of pain requiring 10-12 nitroglycerin tablets per day and by development of recurrent severe paroxysmal nocturnal dyspnea. Coronary arteriography revealed severe disease with multiple constrictions in the small right coronary artery followed by its complete occlusion. There was severe obstructive disease of the left main, the left anterior descending coronary artery and its

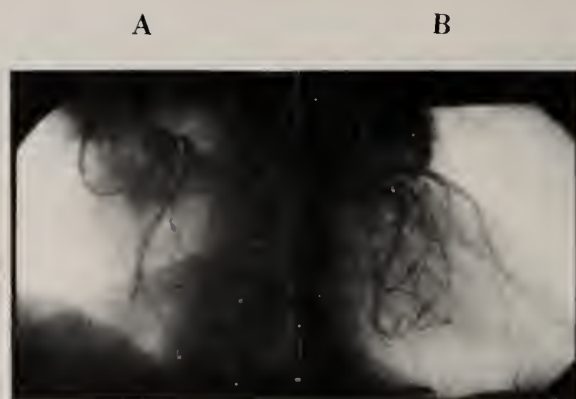


Figure 2 - A is a single frame from the preoperative coronary arteriogram in which the left Sinus of Valsalva was flushed with a Sones catheter. A severe stenosis of the orifice of the left main coronary artery is evident. The tip of the Sones catheter would not enter the coronary artery because of this tight constriction. B is a single frame from the postoperative cine-angiogram showing the saphenous vein graft attached to the root of the aorta and to the left anterior descending coronary artery. Contrast material has been injected through the saphenous vein graft, has filled the left coronary artery, and is seen regurgitating from the proximal end of the left coronary artery into the Sinus of Valsalva. The orifice where the artery arises from the aortic root is seen to be normal in size.

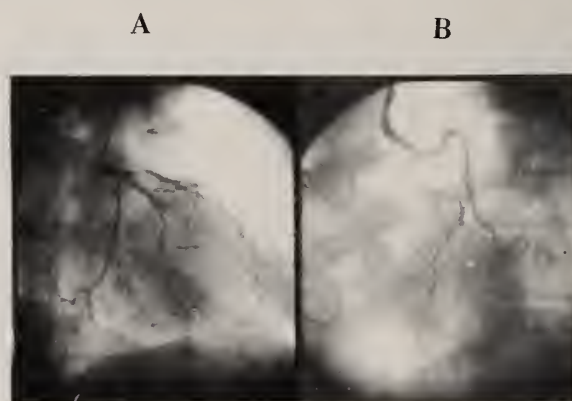


Figure 3 - A is a single frame from the preoperative coronary arteriogram and reveals the lesion in the left coronary artery. B is a single frame from a post-operative coronary arteriogram and reveals the saphenous vein graft from the aortic root to the diagonal branch of the anterior descending coronary artery. An area of constriction in the diagonal branch is seen distal to the anastomosis.

diagonal branch, and the circumflex coronary artery. He was digitalized and myocardial revascularization was done on 5-17-69 as an emergency to prevent myocardial infarction. Saphenous grafts were placed from the aorta to the right coronary artery

and to the left anterior descending coronary artery. Extensive implantation of branches of the internal mammary artery was made into the posterolateral left ventricular wall. Repeat study revealed wide patency of these grafts. The patient has had no angina since operation and continues to work as a judge.

Case Five - N.V.D.H. UWH No. 632570

N. V. D. H., a 44-year old carpenter was admitted for chest pain of three months duration partially relieved by antacids. Two months prior to admission he developed over three to four days a sharp episodic precordial pain which lasted 3-4 minutes, occasionally extended down the inner aspect of the arm to the wrist, and was followed by 45 minutes to an hour of dull pressing precordial pain. Attacks came mostly with exertion but also at times during rest. Seven days before admission he had a recurrence of pain which increased in severity and frequency until it occurred every two hours. The pain was "tight, burning," located centrally in the chest, and radiated into the left arm. On admission to the Intensive Care Unit there was electrocardiographic evidence of posterior wall ischemia. Serum enzymes were not diagnostic of infarction. Emergency coronary arteriograms done because of the unrelenting pain and the presumed high risk of myocardial infarction, revealed severe obstruction of the left anterior descending, diagonal branch of the circumflex, and the right main coronary arteries. No collateral was demonstrated between the two coronary arteries. Because the area of constriction in the right coronary artery was located at the tip of the catheter in the artery the question of induced coronary arterial spasm arose. Coronary arteriograms, repeated 24 hours later, revealed that the right coronary artery was completely obstructed. Its distal portion now filled retrograde through collateral from the left coronary artery. At operation on 5-29-70 there was a grey, fibrin covered area on the anterior wall of the right ventricle which improved considerably in color after nitroglycerin. No clear area of infarction was identified. Saphenous vein grafts were placed from the aorta to the left anterior descending coronary artery and from the aorta to the right coronary artery. The patient was relieved of chest pain, has returned to work and denies any angina since operation.

Discussion

Recent data from pathologic studies of coronary arteries indicate that anatomically it should be possible to bypass the atherosclerotic lesions in 88 percent of hearts of those with coronary atherosclerosis (18). The present emergency myocardial revascularization was successful in four of the five subjects in this report. In the fifth subject myocardial infarction occurred subsequent to repeat coronary arteriography. It is presumed to have occurred in the diagonal branch which was a small vessel and which was constricted by the distal portion of the saphenous vein to coronary artery anastomosis (Fig. 3). Both physician and patient have been reluctant to repeat coronary arteriography to establish where the infarction occurred because the symptoms are predominately those of failure

rather than angina. The four subjects in whom the procedure was successful have been effectively rehabilitated and have returned to their former employment with full vigor.

The bane of preventive medicine is that it is never possible to know in individual subjects when something has been prevented. Consequently it cannot be stated that myocardial infarction has been prevented in any of these subjects. It is clear however from the post-operative angiograms that areas of very significant stenosis in the coronary arteries have been successfully bypassed and the clinical follow-up of the subjects and their exercise tolerance strongly suggests that the new blood supply is effective in relieving myocardial ischemia from localized coronary atherosclerosis. It is believed from the literature that the risk of myocardial infarction is high in subjects with preinfarction angina (19, 20).

In the course of interviewing patients prior to coronary arteriography we have been impressed again and again by striking histories of preinfarction angina which have been ignored and have been followed by myocardial infarction. On coronary arteriography we have frequently found significant proximal lesions which could easily have been by-passed but which have produced major left ventricular myocardial damage. In retrospect it has seemed that many of these subjects might have been saved from serious arrhythmia or major left ventricular destruction by myocardial revascularization. Such cases are a strong indictment of classical therapy for this disease since many subjects are so severely damaged by a single myocardial infarction that they become an invalid with little hope of rehabilitation having insufficient left ventricular myocardium for compensation to occur. Myocardial revascularization for cardiac failure has been generally discouraging whereas relief of pain from ischemia has been generally encouraging. When it is realized that a very significant number of subjects die in their initial attack (13-15) leaving as residue the preceding group it seems reasonable to support the thesis that the optimal time to revascularize a heart is before the first myocardial infarction has occurred. This position seems justified even though the long range course of myocardial revascularization is not as yet known and late fibrosis and obstruction of veins engrafted between the coronary arteries and aorta has been demonstrated (21) as well as progression of the coronary obstructive lesions. Clearly further observations need to be made.

It is of interest in subject number five that in the 24 hour period between two coronary arteriograms there

was clear evidence of collateral from the left to the right coronary artery. On the first occasion the right coronary artery filled completely from its proximal end through an area of tight stenosis but did not fill from the left coronary artery. On the second day the proximal end of the right coronary artery was completely occluded yet its distal end filled from the left coronary artery with contrast material flowing retrograde along the right coronary artery to the site of its proximal occlusion. This phenomenon is not understood at present, and we know of no adequate data concerning the rate of development of collateral in the heart of man. This process (22) has been studied by arteriography in the pig but repeat observations were not made as early as they were in this patient. One of five animals had demonstrated collateral two days after right coronary artery occlusion. In calves the process of opening collateral between the right and circumflex coronary arteries appears to be very rapid (23). It would be interesting to know whether it is as rapid in man.

Summary and Conclusions

1. Classical treatment of angina pectoris and arteriosclerotic heart disease has been accompanied by very significant morbidity and mortality.

2. Many subjects die during their initial myocardial infarction or are left with a badly damaged left ventricle which never again functions adequately to support normal activity.

3. A significant number of subjects have prodromata which can be recognized, and indicate a great risk of developing myocardial infarction.

4. In five subjects presumed to be in the "preinfarction phase," emergency myocardial revascularization has been undertaken.

5. Four of these five subjects have done well and have returned with vigor to their preceding occupation.

Resumen y Conclusiones

1. El tratamiento convencional de la angina de pecho y la cardiopatía arterioesclerosa está asociado con una morbilidad y mortalidad muy significativas.

2. Muchos pacientes mueren como resultado del primer infarto cardíaco o quedan marcadamente incapacitados debido a un ventrículo izquierdo lesionado que no es capaz de funcionar adecuadamente.

3. Un número considerable de pacientes sufren prodromos reconocibles que sugieren que un infarto es

inminente.

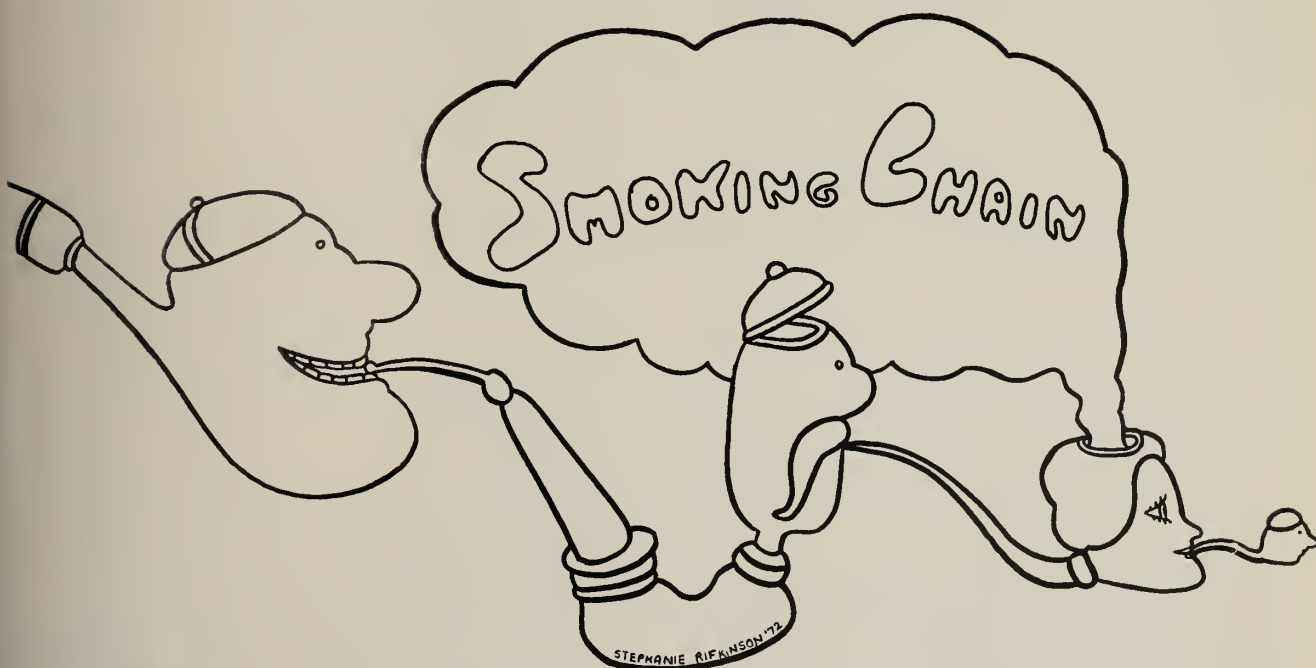
4. Se llevó a cabo revascularización del miocardio como procedimiento de urgencia en cinco pacientes con síntomas y signos de infarto inminente.

5. Cuatro de los cinco pacientes están bien y han regresado a su trabajo.

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DESIGN FOR OLD LIVING. ADVICE ON HOW TO BETTER LIVE WITH IT.

Rafael Rodríguez Molina, MD, FACP

"I will tell you Socrates, he said, what my own feeling is: Men of my age flock together; we are birds of a feather, as the old proverb says; and at our meetings, the tale of my acquaintances commonly is: - I cannot eat, I cannot drink; the pleasures of youth and love are fled away; there was a good time once, but now that is gone, and life is no longer life".

From the Dialogues of Plato: The Republic, Cephalos to Socrates.

As we grow older, we change, some of us more than others, in body and in spirit. There is a tendency to become heavier with body fat changing from perhaps hitherto unseen areas to visible and at times embarrassing ones. A prominent pad of fat frequently appears on the abdomen.

The gait becomes heavier and slower and muscles which not so long ago were hard and rounded gradually become softer, lacking in tone. The desire and will for physical exertion are lessened and daily exercise, particularly for those who have practiced it, is difficult to achieve.

Urination may become more frequent or require stronger effort, particularly in males, while the amount of urine at each micturition is diminished. The odor of body secretions and excretions, such as saliva, sweat, and urine, may become disagreeable and even offensive. While the sexual urge persists, the power, vigor, and ability to consummate diminishes, disappearing completely as time passes by.

Emotionally the aged revert to childhood. An inability to recover from emotional upsets, an increased awareness of physical and mental changes, and frequent states of anxiety are experienced.

Hope and faith weaken and are supplanted by fear and anxiety with thoughts of growing older, of illness, of death, even of suicide, coming to the fore. In fact, old age is a constant deterrent to peace of mind and soul.....

The following is presented as a hedge to what has been said above:

1. Seek the company of younger people, of children.

Keep complaints, aches and pains to yourself. Talk constructively, and smile as much as you can.

2. Maintain cleanliness and neatness of dress; don't forget to dress up every day.

3. Alcohol should be used in moderation and smoking is against the rules. Do not worry about sleeping less and less. Nature will take care of that by allowing you to sleep longer next time.

4. Walk as much as you can, every day, slowly, but erect and gracefully. Be ever careful to avoid falling, particularly while bathing.

5. Lie down after noonmeal, even if you cannot doze, but refrain from remaining too long in bed during the day.

6. Be sure to have your economic problems attended to, and solved, if possible, before you become too old to care.

7. Should your income or family be not in a position to provide extra personal care, nurse or attendant, accept the idea of entering an institution for the care of the aged. While there, make the best of it, trying to adapt yourself to new surroundings, and to new friends.

8. Pray to the Almighty that you do not become a burden to your family. Strive for preserving self-help as long as possible.

9. Refrain from long conversations with family or friends on experiences or achievements of the past. Remember, they are not as interested in hearing them as you are in narrating what, probably you have said many times before.

10. Last, but by no means least important, be prepared to die at any time, in your sleep, on walking, or while talking or being quiet. For death is unavoidable, and as natural as mortal life.

To end this seemingly gloomy and frustrating piece on the subject of aging, our aim is not to scare the young and elderly reader, but rather to inform him or her of certain natural, logical changes that appear in all human beings, as they grow older. In doing this, we wish to urge our medical colleagues to re-assure rather than alarm their elderly patients and friends.

EDITORIAL

CURRENT TRENDS IN CATARACT EXTRACTIONS

The past five years have brought tremendous improvement in our techniques for cataract extraction. As a result, the number of complications have been greatly reduced and the convalescent period has been significantly reduced.

Although this paper is related mostly to the senile type of cataract, many of the improvements are also applicable to the infant patient with cataract.

1. Improvement in suture material.

The gradual reduction in thickness of the various suture materials decreases postoperative inflammation. At present there is a trend towards using 10-0 monofilament, nylon suture material. This material gives a minimal amount of irritation. The corneal epithelium is able to grow over the suture material as is readily observed following a corneal transplant operation. Absence of irritation permits the use of a running interlock, buried, type of suture. This type of wound closure has reduced the incidence of shallow and flat anterior chambers that occasionally complicated cataract extractions with previous techniques. Buried sutures means that the conjunctiva covers the sutures completely and therefore the patient does not experience a foreign body sensation.

2. Improvements in visual aids.

The routine use of the operating microscope allows a more exact placement and closure of the surgical wound, a routine necessary for placement of 10-0 monofilament suture. For those reluctant to adapt themselves to the use of the operating microscope, the development of finer optical loupes has been helpful.

3. Reducing the length of the wound.

With the introduction of better cryoprobes the extraction of the lens is now possible through a 130 - 140° wound routinely. The newer cryoprobes are thinner and rapidly able to thaw thus allowing extraction to occur thru a smaller opening since the complication of rupturing the capsule are reduced. Both the amount of surgically induced astigmatism and the incidence of wound leak with flat chambers have diminished; reduction in the total length of the wound is the main reason.

4. Improvement in the instruments to remove the lens.

The cryoprobes especially those designed to allow rapid thawing, have reduced the incidence of capsule rupture. The probes have practically eliminated injury to the corneal endothelium, previously produced by either the erisophake or the capsule forceps. Because of the strong hold to the lens, the need for alpha-chymotrypsin to dissolve the zonules has diminished. By avoiding the use of the enzyme the cornea is kept crystally clear and the possibility of enzyme induced glaucoma and bullous keratopathy are eliminated.

5. Osmotic agents to lower the intracapsular pressure.

The pre-operative use of intravenous mannitol has decreased the incidence of vitreous loss by lowering the intraocular pressure. We prefer administration of 200 cc of a 20 percent mannitol solution, 90 minutes prior to surgery.

6. Anterior vitrectomy for vitreous loss.

If vitreous loss occurs during the procedure, anterior vitrectomy should be performed so as to avoid the complication of retinal detachment, updrawn pupil, secondary glaucoma and persistent inflammation of the iris, vitreous and retina. The vitrectomy should be performed so as to clear the whole anterior chamber of vitreous but should not be done too extensively in order to avoid a retinal detachment and cystoid macular changes.

7. Elimination of long acting mydriatics and eye patch.

Due to the use of smaller incisions and better tolerated suture materials, the iritis is minimal, thus the use of long acting mydriatics like atropine seldom becomes necessary for more than one to two weeks after surgery. Eye patches are not used after the first week for the same reasons.

8. Round pupil technique.

Due to the development of better tolerated contact lenses, it has become preferable to extract the lens through an intact round pupil. In Puerto Rico this is of particular importance since the sunlight produces photophobia in patients with pupils other than the normal round pupil. The newer cryoprobes have allowed us to safely extract a cataract through a round pupil.

9. Anesthesia.

With the use of the operating microscope and the need for the patient to remain steady in one position, anesthesiologists now prefer profound basal anesthesia, or general anesthesia. An advantage of general anesthesia using halothane derivatives, is that the paralysis of the extraocular muscles reduces the intraocular pressure and therefore the chances of vitreous loss.

10. Use of antibiotics.

There is definite evidence, at the present, that the incidence of postoperative endophthalmitis has been diminished by the use of subconjunctival antibiotics at the end of the surgical intervention. The use of preoperative topical antibiotic therapy as well as routine bacteriological conjunctival cultures is still a debatable argument.

In summary, all the changes mentioned above have provided the ophthalmologists with tools that have significantly reduced the number and degree of cataract surgery complications during and after the procedure.

José Berrocal, MD

National Congress on the Quality of Life March 22-25, 1972 Palmer House/Chicago, Illinois



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Before

3/29/67 Before therapy with 5%-FU cream. Patient P.T. shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

After

6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.





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al it actinic, solar or senile keratoses,
may regard it as "precancerous."^{1,2}

ical fluorouracil, considered by some dermatologists to be a major
lance in the treatment of multiple solar keratoses,^{3,4} offers the physi-
a relatively inexpensive alternative to cryosurgery, electrodesic-
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Efudex offers 2% and 5% solution and 5% cream formulations—formula-
ons that have proved effective in the treatment of these mutiple lesions.

usual duration of therapy, 2 to 4 weeks.

udies showed that with the 2% and 5% Efudex preparations, the usual
rtion of therapy was only 2 to 4 weeks.⁵ Other studies with topical
ouracil revealed that when concentrations of less than 2% were
e significant numbers of lesions recurred.⁶

rats the lesions you can't see, too.

uerous lesions, not apparent prior to 2% and 5% Efudex therapy,
a fested themselves by definite reactions, while intervening skin
ained relatively unaffected.⁵ The early eradication of these subclini-
lions (which may otherwise have undergone further progression)
ably accounts for the reduced incidence of future solar keratoses in
tnts treated with topical fluorouracil—especially with 5%
ntrations.⁶

ov to identify solar keratoses.

ically, the lesion—a flat or slightly elevated brown to red-brown
ple—is dry, rough, adherent and sharply defined. Multiple lesions
he rule.

redictable therapeutic response.

response to a typical course of Efudex therapy is usually
acteristic and predictable. After 3 or 4 days of treatment, erythema
gins to appear in the area of keratoses. This is followed by a moderate
dense inflammatory response, scaling and occasionally moderate
erness or pain. The height of this response generally occurs two
es after the start of therapy and then begins to subside as treatment
opped. Within two weeks of discontinuing medication, the
lammation is usually gone. Lesions that do not respond should
opsied.

ferences: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York,
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Da on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and
rE.: *Cancer*, 25:450, 1970.

Before prescribing, please consult
complete product information, a summary of
which follows:

Indications: Multiple actinic or solar
keratoses.

Contraindications: Patients with known
hypersensitivity to any of its components.

Warnings: If occlusive dressing used,
may increase inflammatory reactions in
adjacent normal skin. Avoid prolonged expo-
sure to ultraviolet rays. Safe use in pregnancy
not established.

Precautions: If applied with fingers, wash
hands immediately. Apply with care near eyes,
nose and mouth. Lesions failing to respond or
recurring should be biopsied.

Adverse Reactions: Local—pain, pruri-
tus, hyperpigmentation and burning at
application site most frequent; also dermatitis,
scarring, soreness and tenderness. Also
reported—insomnia, stomatitis, suppuration,
scaling, swelling, irritability, medicinal taste,
photosensitivity, lacrimation, leukocytosis,
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Dosage and Administration: Apply
sufficient quantity to cover lesion twice daily
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Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop
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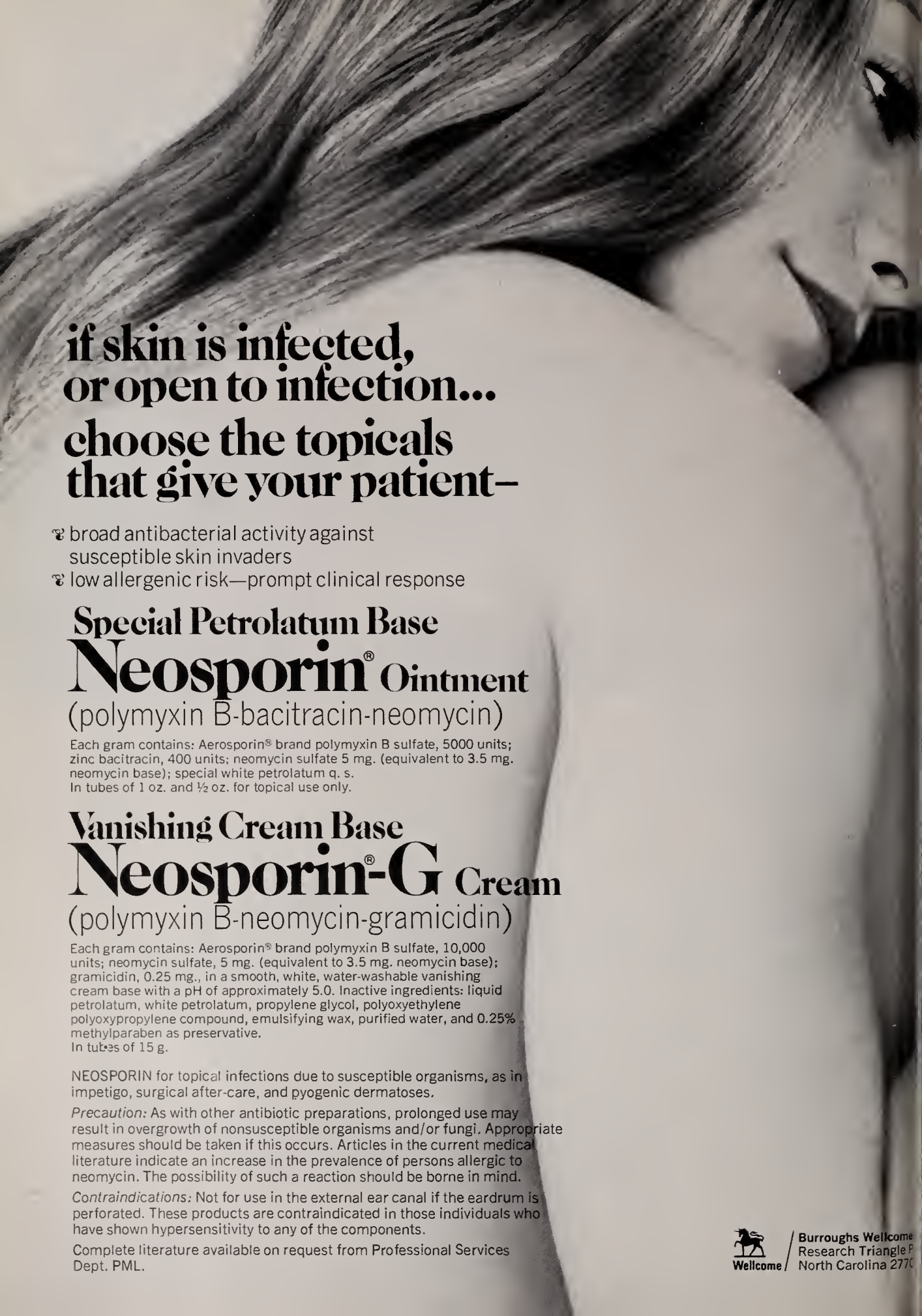
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Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures.

Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision.

Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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ON EUTHYROID CORONARY SUBJECTS – FINAL REPORT 64

Elí A. Ramírez, MD, MS, P. H. García Pont, MD and Frankie Alvarado Norat, MD

EN TORNO A LA FIEBRE REUMATICA 74

Felipe Vizcarrondo, MD y Amalia Martínez Picó, MD

THE TOXICOLOGY OF ASPIRIN 78

Sidney Kaye, MSc, PhD

EFFECTIVENESS OF MINOCYCLINE IN BACTERIAL INFECTION 81

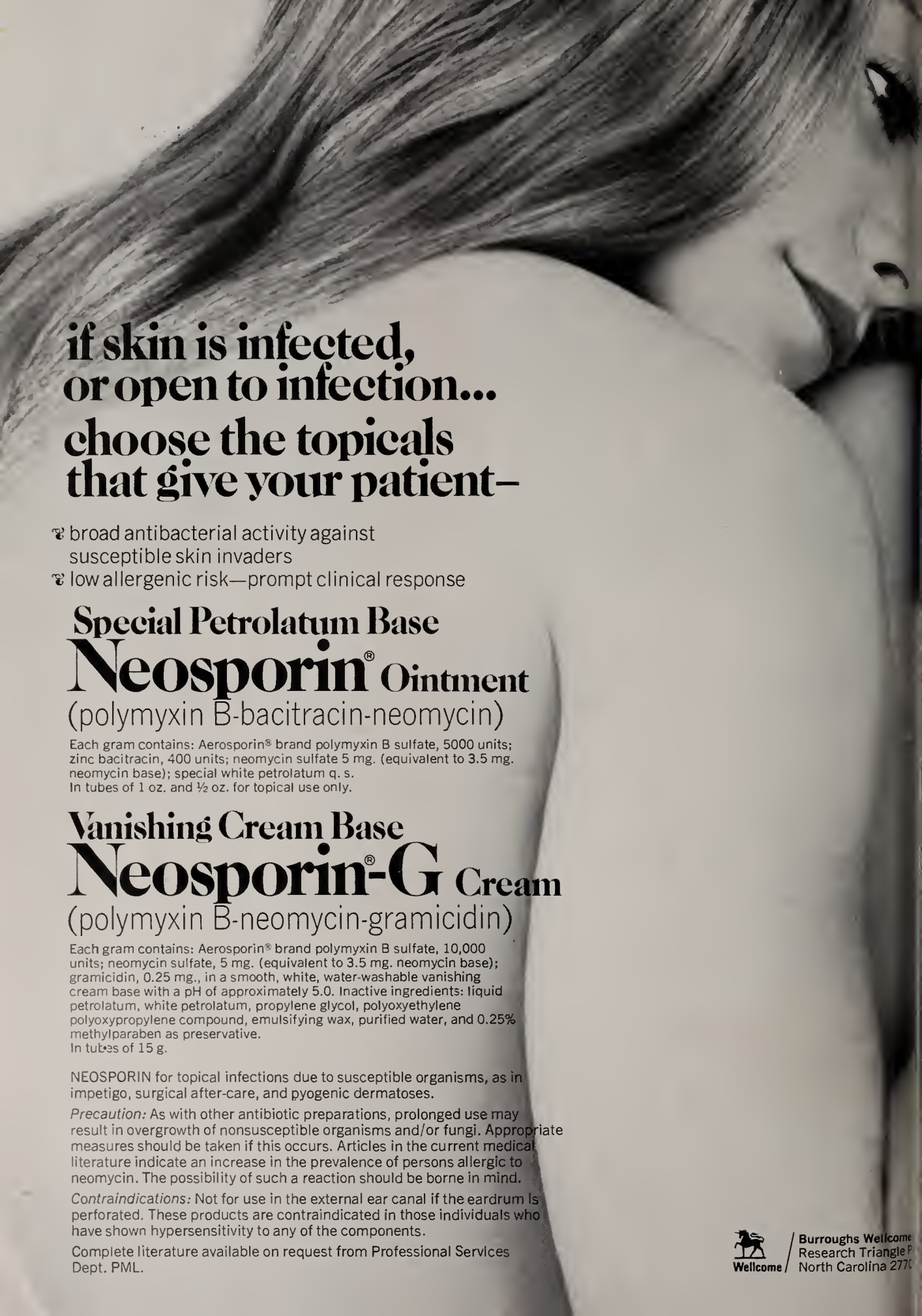
Lillian Conde Pérez, MD

EDITORIAL 84

Utilization, Nuisance or Necessity?

CARTA A LA REDACCION 86

NOTICIAS 87



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In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

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Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

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Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close observation. Obtain a detailed history, and complete physical and laboratory examination (complete blood count, urinalysis, etc.) before prescribing and at regular intervals thereafter. Carefully select patients, including those responsive to routine measures, complicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Tablets should be taken with meals or a full glass of water. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral ulcers (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or loss. A one-week trial period is adequate. Discontinue the drug at the first sign of a favorable response. Restrict alcohol intake to one week in patients over sixty. **Indications:** Acute gouty arthritis, rheumatoid arthritis, ankylosing spondylitis. **Contraindications:** Children 14 years or less; senile debility; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent peptic ulcers; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypotension; thyroid disease; systemic edema; glaucoma; and salivary gland enlargement due to the drug. **Warnings:** Polymyalgia rheumatica and temporal arteritis may be receiving other potent chemotherapeutic agents or long-term anticoagulant therapy. **Precautions:** Age, weight, dosage, duration of therapy, and presence of concomitant diseases, and concurrent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use the lowest effective dosage. Weigh initially and frequently to detectable benefits against potential risk of severe, untoward, reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

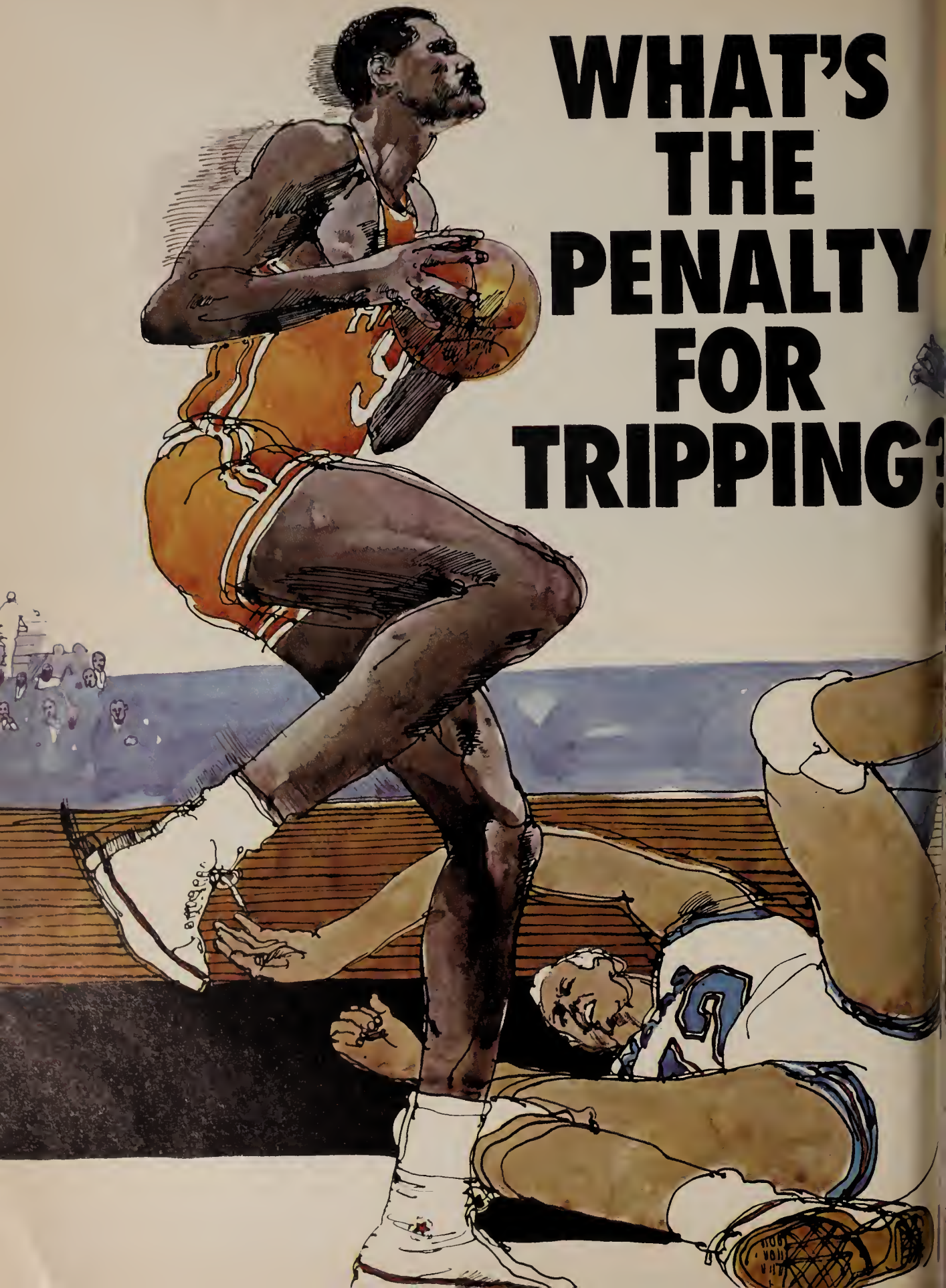
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B) 98-146-800-E

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

WHAT'S THE PENALTY FOR TRIPPING?



A personal foul against the tripper, and possibly weeks of painful skeletal muscle spasm for the victim.

For the skeletal muscle spasm of leg strains, Valium® (diazepam) can be a valuable adjunct. A dose of 2-10 mg, three or four times a day, goes to work to help break up the cycle of spasm/pain/spasm. The resultant relief of skeletal muscle

spasm may permit greater mobilization of the affected muscles and may help the patient resume usual activities sooner than otherwise possible.



Sudden trauma to and unusual stress on sartorius muscle may cause strain of muscle and tearing of some of the fibers. The resultant muscle spasm can make leg motion painful.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

VALIUM® (diazepam)

adjunct in skeletal muscle spasm

2-mg, 5-mg, 10-mg tablets



To get the water out
in edema*

To lower blood pressure
in hypertension*

To spare potassium
in both

There's

Dyazide[®] Trademark

Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Before prescribing, see complete prescribing information in SK&F literature or PDR.

***Indications:** Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome, late pregnancy; also steroid-induced and idiopathic edema, and edema resistant to other diuretic therapy. 'Dyazide' is also indicated in the treatment of mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., certain elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—they can both cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia

have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules.

SK&F CO.

Carolina, P.R. 00630
a subsidiary of Smith Kline & French Laboratories

**This is no time for his
stomach to be on his mind...**

Effective Maalox keeps his
stomach at ease.
Pleasant flavored suspension
or tablets. Does not cause
constipation.

MAALOX[®]

(Magnesium-Aluminum Hydroxide)

William H. Rorer, Inc.

Fort Washington, Pa., U.S.A.



What it means to live and work in Tipton County, Tennessee

**Persons who are white and
over 40 have one chance in four
of having solar keratoses...
which may be premalignant**

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

**Prevalence of solar keratoses in white persons
over 40 in Tipton County, Tennessee**

Female	159	44
Male	117	66

☐ Persons without solar keratoses ☒ Persons with solar keratoses

*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



lar, actinic, senile keratoses

ed by many names, the typical lesion is flat
ightly elevated, brownish or reddish in
r, papular, dry, adherent, rough, sharply
ed; usually multiple lesions, chiefly on
sed portions of the skin.

quence/selectivity of response

shema in areas of lesions may begin after
al days of therapy; height of reaction
v in affected areas)* usually occurs within
weeks, declining after discontinuation of
apy. Since this response is so predictable,
ns that do not respond should be biopsied
le out the presence of a frank neoplasm.

smetic results

smetic results are highly favorable. Inci-
e of scarring is low—important with multi-
cial lesions. Efudex should be applied
care near the eyes, nose and mouth.

cream—a Roche exclusive

Roche formulates the 5% cream...
n patient acceptability...high in clinical
cy, especially for lesions of hands and
rms...economical.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

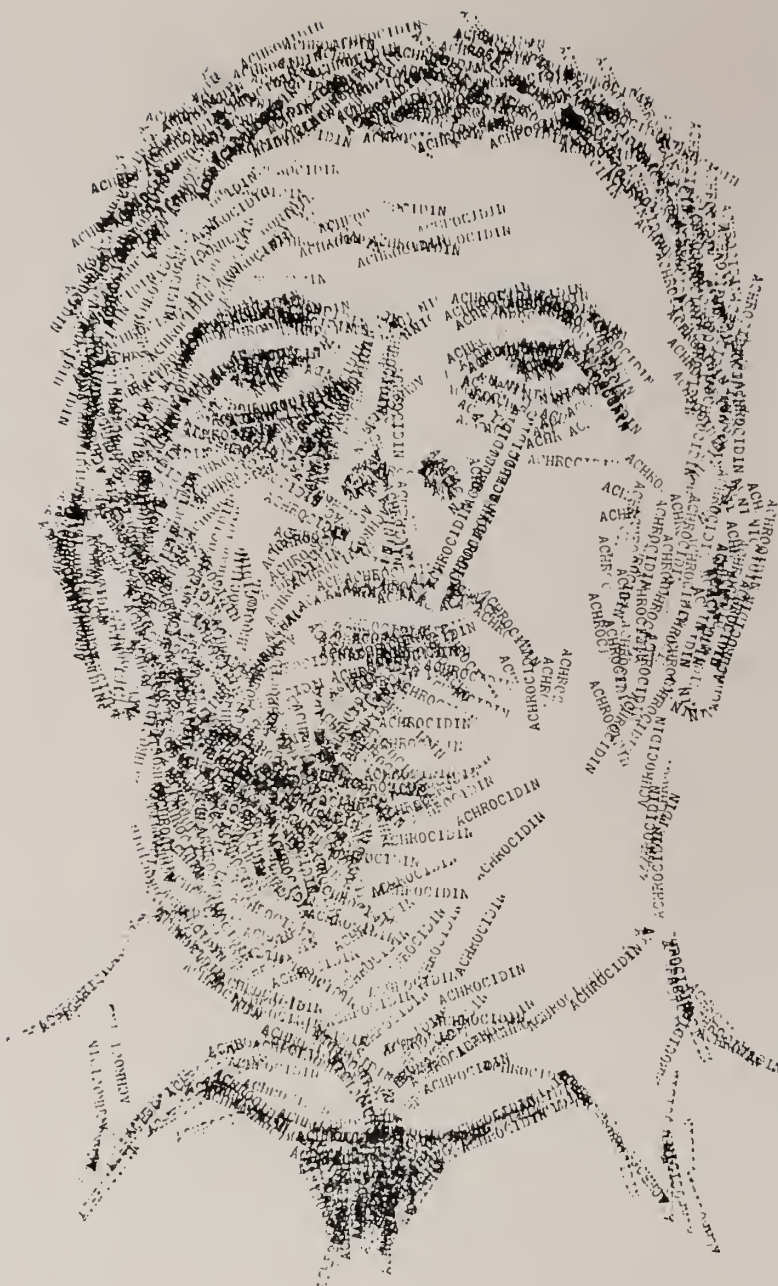
Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

an alternative to conventional therapy **Efudex[®]** (fluorouracil) cream/solution



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110





Achrocidin[®] Tablets and Syrup

Tetracycline HCl—Antihistamine—Analgesic Compound

Each tablet contains: ACHROMYCIN[®] Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Caffeine 30 mg.; Salicylamide 150 mg.; Chlorothen Citrate 25 mg.

ACHROCIDIN Tetracycline HCl—Antihistamine—Analgesic Compound Tablets and Syrup are recommended for the treatment of tetracycline-sensitive bacterial infection which may complicate vasomotor rhinitis, sinusitis and other allergic diseases of upper respiratory tract, and for the concomitant symptomatic relief of headache and nasal congestion. For children and elderly patients you may prefer caffeine-free **ACHROCIDIN** Syrup. Each 5 cc contains: **ACHROMYCIN** Tetracycline equivalent Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Salicylamide 150 mg.; Ascorbic Acid (C) 25 mg.; Pyrilamine Maleate 15 mg.

Contraindications: Hypersensitivity to any component.

Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.

Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons

on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculo-

popular and erythematous rashes; exfol dermatitis; photosensitivity; onycholysis discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Tooth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestatic jaundice, high dosage.

Upon adverse reaction, stop medication and treat appropriately.



LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York 10965

¿Habla español?

not, the new Rocom Health History Questionnaire asks questions in Spanish...

provides answers in English

- | | | | |
|--|-----|--|--|
| ¿Le molestan coyunturas o músculos rígidos o dolorosos? | 1. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Se le hinchon las coyunturas? | 2. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Le molestan dolores en la espalda u hombros? | 3. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Le duelen los pies con frecuencia? | 4. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Está desahilitado en alguna manera? | 5. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Tiene algún problema con su piel? | 6. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Le pica o quema la piel? | 7. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Sangra por largo tiempo cuando se hace una pequeña cortadura? | 8. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Se lastima fácilmente formando un cardenal o morete? | 9. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Se ha desmayado o se ha sentido como que se va a desmayar? | 10. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Tiene alguna parte del cuerpo siempre adormecida? | 11. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Ha tenido alguna vez convulsiones? | 12. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Le ha cambiado últimamente su letra al escribir? | 13. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Tiene tendencia a temblar o menearse mucho? | 14. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Se pone nervioso en presencia de personas extrañas? | 15. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Se le hace difícil tomar decisiones? | 16. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Se le hace difícil concentrar o recordar? | 17. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Se siente solo o deprimido? | 18. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Llora a menudo? | 19. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Diría usted que tiene una perspectiva irremediable? | 20. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Tiene dificultad en relajar o reposar? | 21. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Tiene a preocuparse demasiado? | 22. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Le molestan o asustan algunos sueños o pensamientos? | 23. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Tiene a ser tímido o sensitivo? | 24. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Se molesta mucho cuando lo critican? | 25. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Pierde el genio con frecuencia? | 26. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Cosas pequeñas lo hacen molestar? | 27. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |
| ¿Le molesta cualquier trabajo o problemas familiares? | 28. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Tiene algún problema con su vida sexual? | 29. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Ha considerado alguna vez suicidarse? | 30. | Sí <input type="checkbox"/> | No <input checked="" type="checkbox"/> |
| ¿Ha descado alguna vez, o buscado, ayuda psiquiátrica? | 31. | Sí <input checked="" type="checkbox"/> | No <input type="checkbox"/> |

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13. MUSCULOSKELETAL

- ☒ aching muscles or joints
- ☐ swollen joints
- ☒ back or shoulder pains
- ☐ painful feet
- ☐ handicapped

14. SKIN

- ☐ skin problems
- ☐ itching or burning skin
- ☐ bleeds easily
- ☐ bruises easily

15. NEUROLOGICAL

- ☒ faintness
- ☒ numbness
- ☐ convulsions
- ☐ change in handwriting
- ☐ trembles

16. MOOD

- ☒ nervous with strangers
- ☒ difficulty making decisions
- ☒ lack of concentration or memory
- ☐ lonely or depressed
- ☐ cries often
- ☐ hopeless outlook
- ☒ difficulty relaxing
- ☒ worries a lot
- ☐ frightening dreams or thoughts
- ☒ shy or sensitive
- ☒ dislikes criticism
- ☒ loses temper
- ☒ annoyed by little things
- ☐ work or family problems
- ☐ sexual difficulties
- ☐ considered suicide
- ☒ desired psychiatric help

When your patient speaks little English and your Spanish is limited or nonexistent, you need the new Rocom Health History Questionnaire (Spanish).*

The uniqueness of this new Rocom system lies in the fact that the questions are asked in *Spanish*, but you read the answers in *English*. The form itself does the "translating."

You have to see it yourself to appreciate the ease and completeness of this new history-taking technique, which includes questions covering all body systems.

Designed and developed by Patient Care Systems, Inc.

For information about the new Rocom Health History Questionnaire (Spanish) and other components in the Rocom Medical Management System, please fill out the coupon and send it to us.

Name

Specialty

Address

City State Zip

U

MMS - 1H

HE Rocom™ Division of Hoffmann-La Roche Inc.
Box 169, Fairview, New Jersey 07022

We're not against all her E.coli...

only the E.coli in her
urinary tract



Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. *And it does not suppress normal bac-*

**Basic in cystitis*, pyelitis*,
pyelonephritis***

The one-tract action of

Macrochantin® Capsules
(nitrofurantoin macrocrystals) 50mg./100mg

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterra-

nean and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus or Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise, muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulopenia, has been reported rarely. The blood picture returned to normal following cessation of therapy with other antimicrobial agents, superinfection with resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.
Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg.
EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04).



Originators and Developers of The Nitrofurantoin
EATON LABORATORIES
Norwich International
410 Park Avenue, New York, N.Y. 10022

A 5 YEAR DOUBLE BLIND CONTROLLED CLINICAL TRIAL OF D-THYROXINE ON EUTHYROID CORONARY SUBJECTS— FINAL REPORT

Elí A. Ramírez, MD, MS
P. H. García Pont, MD
Frankie Alvarado Norat, MD

The control of hypercholesterolemia is generally regarded today as one of the most promising approaches to the prevention of atherosclerotic disease. This hope is based principally on the relationship found throughout the world by epidemiologic investigators (1, 3) between the serum cholesterol and the prevalence of coronary artery disease. The strength of this relationship has been reinforced by the discovery in several prospective studies (2) that the serum cholesterol is a potent predictive factor for overt atherosclerotic complications.

That the serum cholesterol is related and subject to dietary control was suspected in the original epidemiologic investigations (3). Subsequently, this relationship was strengthened by the demonstration that effective reduction of the serum cholesterol can be accomplished through dietary fat restriction (4, 5). It has been also demonstrated that the serum cholesterol can be effectively reduced by various pharmacologic agents (6, 7, 8).

There are already several studies which suggest that it may be possible to prevent atherogenesis through the reduction of the serum cholesterol (9, 10). However, the issue is far from settled. Even though this effect may be eventually demonstrated to everyone's satisfaction, there are several considerations such as the protracted course of the disease, the multiplicity and variability of the various risk factors, the problems involved in long term management, etc., that indicate caution in the interpretation of the results. It may well take many years of carefully designed investigations to reach definitive answers to the questions.

One of the most important practical problems in the therapeutic management of any chronic disease such as atherosclerosis is the difficulty in obtaining patient cooperation in following long term regimes. Almost

everyone will agree that this is particularly true for dietary management (9). An example is the common experience that diabetics by and large prefer taking some form of oral medication to having to conform to a restricted dietary pattern. Another practical problem that concerns atherosclerosis in particular is that until screening programs become more effective, most patients will continue to come to the physicians' attention after they have already developed a complicating event indicative of advanced disease.

The present study was designed to explore the effectiveness of a hypocholesterolemic regime in a clinical setting in which it would be ordinarily considered to be indicated. Subjects were selected for treatment after they had had a proven coronary event regardless of their serum cholesterol level. D-Thyroxine was chosen as the hypocholesterolemic agent because it avoided the dietary adherence problem and a preliminary investigation indicated that it is appropriate for long term administration to known coronary subjects (11). For our purposes it has the additional advantage that it appears to be specially effective in controlling the hypercholesterolemia associated with the Fredericksen type II lipoprotein abnormality which predominates in patients with clinical coronary atherosclerotic disease (12).

When administered orally, D-Thyroxine is rapidly absorbed directly into the blood and is concentrated in the liver. The agent produces a hypocholesterolemic response comparable to that of L-Thyroxine. The effect of D-Thyroxine upon cholesterol apparently consists of increasing its oxidative catabolism with excretion of the resultant products through the biliary system (13, 14).

A practical limitation to D-Thyroxine therapy is its small but nevertheless significant hypermetabolic effect. This effect may be acceptable on a short term basis, but might render the drug undesirable for long term use. Precisely, those patients in whom the treatment most frequently would be considered to be indicated, the known coronary subjects, would be the ones expected to be most affected by this potential hazard.

Based on the above considerations, the present study

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was designed to accomplish the following objectives:

1) To determine if long term hypocholesterolemic therapy with D-Thyroxine is feasible for coronary subjects under a clinical setting in which such therapy would be frequently considered to be indicated.

2) To determine if coronary subjects who already have developed overt clinical manifestations of their disease can tolerate the calorogenic effects of this drug on a long term basis, at a dose expected to produce an effective hypocholesterolemic response.

3) To determine if this form of therapy results in a decrease of the morbidity and mortality of the disease under the circumstances described.

Materials and Methods

All patients were male veterans admitted to the San Juan Veterans Hospital.

Requisites for acceptance were definite evidence of myocardial necrosis at least three months before randomization, willingness to cooperate and ability to stay under prolonged follow up. Age above 70 years, an etiology for heart disease other than atherosclerosis or hypertension, and a diagnosis of another disease carrying an unfavorable prognosis for life within a 5 years period were reasons for exclusion.

As noted above, no attempt was made to select hypercholesterolemic individuals. No special diets or other hypocholesterolemic treatment was given. Treatment for cardiac and other conditions was prescribed as needed.

The baseline examinations included a complete history and physical examination, serum lactic dehydrogenase, serum glutamic oxalacetic and pyruvic transaminases, fasting blood sugar, blood urea nitrogen, alkaline phosphatase, serum uric acid, inorganic phosphorus, PA chest X-ray, hematocrit, white blood cell and differential counts, urinalysis, 12 lead electrocardiogram, I 131 uptake, and Triiodothyronine (T_3) RBC uptake. The serum cholesterol was determined according to the method of Zak (15) tested daily against standard controls. Beta-lipoprotein was determined according to the Immunocrit method (16).

At the completion of the baseline examination all patients were randomized using an envelope method into either a D-Thyroxine or a placebo treated group. The randomization was arranged to enable pairing for sequential analysis. D-Thyroxine and its identical placebo were coded under six different numerical lots. The dosage was one 2 mg. tablet twice a day. This dosage was selected on the basis of previous observations (11) which indicated that it could accomplish approximately a 10 percent hypocholesterolemic response in unselected subjects. It was also expected to avoid potentially hazardous hypermetabolic effects in coronary disease patients.

The patients were followed at a special clinic every three months. At that time an interval history, a physical examination and a side effects interview were performed. In addition, the serum cholesterol, beta-lipoprotein, Triiodothyronine (T_3) RBC uptake, fasting blood sugar, blood urea nitrogen and serum uric acid were determined. Every year the baseline

evaluation was repeated.

The treatment was continued until either an end point of new myocardial infarction occurred, a clinical picture developed which in the opinion of the authors made hazardous the continuation of treatment, the patient dropped out of treatment for other reasons, or five years of treatment were completed. Decisions regarding the achievement of end points and the discontinuation of treatment were reached without knowledge of the treatment given. In order to preserve the double blind design the medication codes, the sequential pair data, the serum cholesterol values, and the thyroid functional data were kept in a file separate from the patient's record.

Statistical data analysis was performed using standard methods (17). Differences with probabilities greater than $p=0.05$ were not considered significant.

Results

Seventy one patients were randomized: 38 on placebo treatment and 33 on D-Thyroxine. (In all tables Sodium D-Thyroxine is abbreviated as DT₄.)

Baseline Data:

Baseline qualitative data are shown on table I. No significant differences were found in the characteristics listed between the two groups.

Baseline quantitative data are shown in table II. There was no difference between the placebo and D-Thyroxine treated groups in age, period elapsed since the myocardial infarction, serum cholesterol, beta lipoprotein, blood urea nitrogen, fasting blood sugar, I 131 thyroid uptake and triiodothyronine (T_3) RBC uptake. However, the initial average body weight of the D-Thyroxine treated group was significantly lower than that of the placebo treated group at $p < 0.05$ level.

TABLE I: BASELINE QUALITATIVE DATA ON PATIENTS CLASSIFIED ACCORDING TO TREATMENT RECEIVED (DT-4 = SODIUM D-THYROXINE). SEE TEXT.

	GROUP CHARACTERISTICS	
	BASELINE QUALITATIVE DATA:	
	Placebo 38 PTS	DT-4 33 PTS
History of CHF *	6	7
Diastolic BP > 90	15	6
History of Angina	18	21
Arteriosclerosis Obliterans	0	3
Cerebrovascular Insufficiency	2	1
Diabetes	7	1

* - CHF means Congestive Heart Failure.

TABLE II: BASELINE QUANTITATIVE DATA ON PATIENTS CLASSIFIED ACCORDING TO TREATMENT RECEIVED. (*) ASTERISK INDICATES A SIGNIFICANT DIFFERENCE BETWEEN THE MEANS AT LEVEL OF $P < .05$

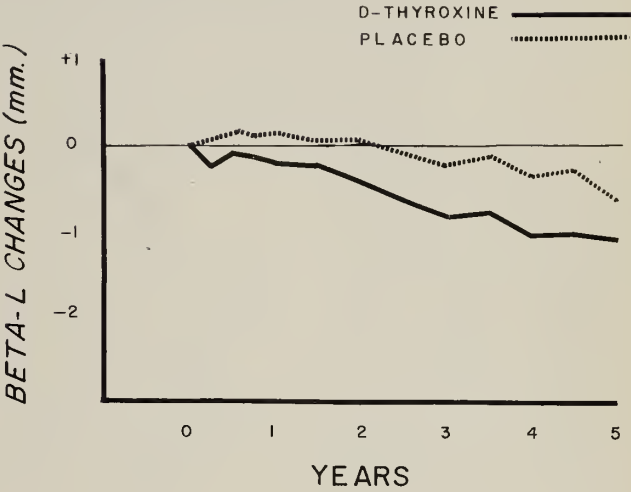
GROUP CHARACTERISTICS		
BASELINE QUANTITATIVE DATA:		
	Placebo 38 PTS	DT-4 33 PTS
Age (Yrs.)	51.1	53.84
Weight (Lbs.)	166.55	152.15
Period since M. I. (MOS.)	18.15	16.27
Cholesterol (mg. percent)	204.61	211.32
Beta Lipoprotein (MM.)	2.934	2.928
I ₁₃₁ Thyroid Uptake (Percent)	17.2068	16.48
Tri-Iodothyronine RBC Uptake (Percent)	14.22	13.656
Serum Uric Acid (mg. percent)	6.342	5.936
B. U. N. (mg. percent)	11.802	11.545
F. B. S. (mg. percent)	94.4	87.55



Graph I. Serum cholesterol changes in mg. percent in D Thyroxine and placebo treated patients.

There is no apparent selective basis for this finding which is believed to be due to chance in the sampling distribution.

Changes in baseline variables during 5 years of follow up:

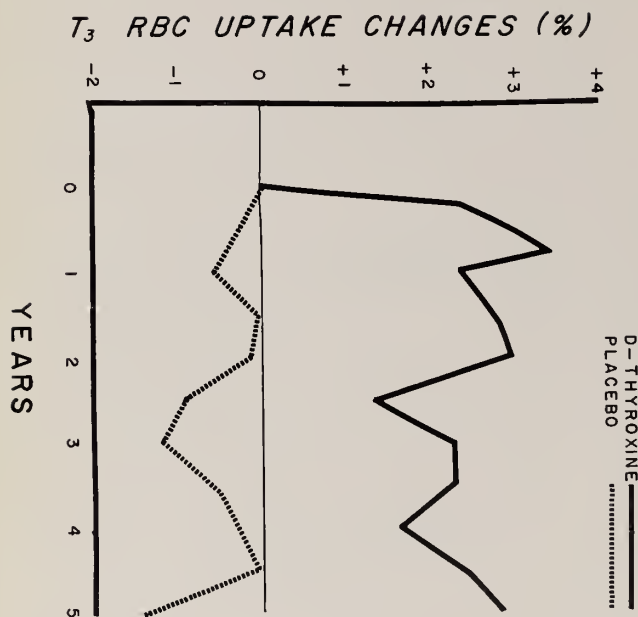


Graph II. Beta lipoprotein changes in mm. of precipitate in D Thyroxine and placebo treated patients.



Graph III: 24 hr. I₁₃₁ thyroid gland uptake in D Thyroxine and placebo treated patients.

The number of patients included in the graphs diminishes gradually according to the losses due to end point events over the 5 years period of observation. At the end there remained 19 patients in the placebo treated group and 20 patients in the D-Thyroxine



Graph IV. Tri-iodothyronine (T_3) RBC uptake in D Thyroxine and placebo treated patients.

treated group.

Serum cholesterol changes during 5 years of follow up are shown in graph I. The serum cholesterol was lower in the D-Thyroxine treated group at all periods after the initial determination. However, the difference was not significant at a level of $p < 0.05$ until 18 months after the start of treatment. The difference remained significant at all subsequent periods.

Beta lipoprotein changes during five years of follow up are shown in graph II. The D-Thyroxine treated group showed significantly lower Beta lipoprotein values at p levels less than 0.05 at all annual checks.

The changes in 24 hr. I^{131} uptake by the thyroid gland are shown in graph III. There was a significant decrease in uptake in patients on active treatment at all annual checks.

The changes in triiodothyronine (T_3) RBC uptake are shown in graph IV. This was significantly elevated in patients on active treatment at all checks.

No significant differences were noted between D-Thyroxine and placebo treated patients in blood urea nitrogen, fasting blood sugar, serum uric acid, blood counts, hematocrit, serum lactic dehydrogenase, serum glutamic oxalacetic and pyruvic transaminases, and serum alkaline phosphatase throughout the 5 years of observation.

Side Effects:

The subjective side effects were evaluated at each clinic visit through personal interviews using a check list. The evaluation was based on the comparison of the res-

ponse at the moment of the interview with the pre-treatment response. Observations were classified according to the subjective reaction as either better, same, or worse. The specific items checked were pre-existing angina, newly acquired angina, sweating, nervousness, appetite change, body weight and palpitations. The results are shown in table III.

Pre-existing angina:

Pre-existing angina was evaluated as to its severity, duration of episodes, and frequency. For each treatment the number of "worse" vs. "same" or "better" responses were entered into an appropriate Chi square table for analysis. In all three aspects there were significantly more "worse" responses from D-Thyroxine treated patients than from placebo treated patients. The levels of significance were $p < 0.02$ for duration of episodes, $p < 0.05$ for frequency of attacks, and $p < 0.05$ for severity of pain.

New angina:

Newly acquired angina was evaluated on the basis of incidence of complaints after start of treatment. There was no significant difference between both groups.

Diarrhea:

Diarrhea was evaluated on the basis of the number of diarrheic episodes during the observation period. There was a significantly higher frequency of complaints of diarrhea in the D-Thyroxine treated group than in the placebo group.

Other subjective side effects:

The Chi square analyses of the remaining subjective side effects (sweating, tremors, nervousness, appetite change and palpitations) did not show significant differences between both groups.

Pulse rates:

Pulse rates were determined at each clinic under uniform conditions for both groups of patients. When compared to the baseline values no significant differences were observed between both groups.

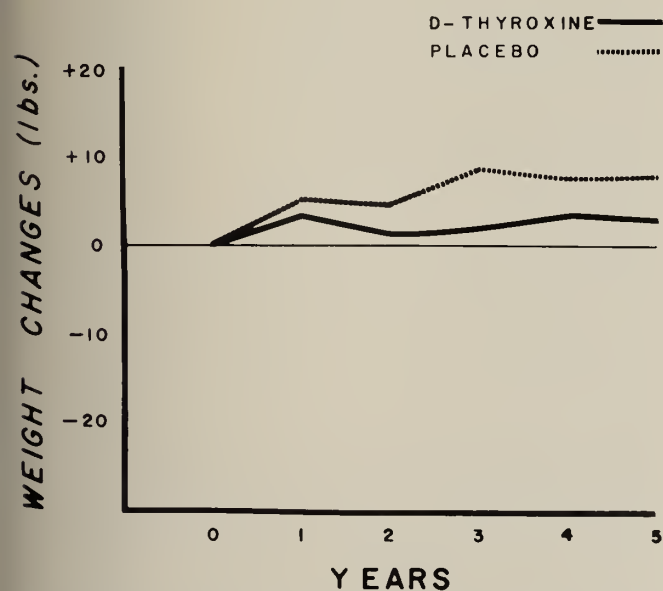
Electrocardiographic changes:

Except at the time of development of frank ischemic complications no remarkable electrocardiographic changes were observed. Besides the yearly routine electrocardiograms, frequent tracings were performed at clinic visits according to the usual indications such as chest pain, palpitations, etc. In retrospect this was required no more frequently in one group than the other and no particular differences in electrocardiographic findings was observed at these times.

Body weight:

TABLE III: SUBJECTIVE SIDE EFFECTS EVALUATED AS RESPONSES UPON CLINIC INTERVIEWS COMPARED WITH THE PRE TREATMENT RESPONSE IN D-THYROXINE AND PLACEBO TREATED PATIENTS. (*) ASTERISK INDICATES SIGNIFICANT DIFFERENCES AT LEVELS OF $P < .05$ OR LESS. SEE TEXT.

	SUBJECTIVE SIDE EFFECTS			
	PLACEBO		D-THYROXINE	
	Worse	Not Worse	Worse	Not Worse
1. Pre-existing angina				
Severity	23	131	64	163 *
Duration	23	131	57	162 *
Frequency	28	126	61	156 *
2. New angina	15	184	4	111
3. Diarrhea	17	371	42	321 *
4. Sweating	91	297	92	271
5. Nervousness	75	313	92	271
6. Appetite change	61	337	47	337
7. Palpitations	69	319	80	283



Graph V. Change in body weight during 5 years of treatment in D Thyroxine and placebo treated patients.

As was stated before, the initial average body weight was significantly lower at the start of treatment in the D-Thyroxine group than in the placebo treated group ($p < 0.05$). In the absence of any recognizable selective factor, it is believed that this difference is probably due to chance in the sampling distribution. In any case, the difference in initial weight does not affect the analysis of the data because the change in body weight rather than the weight itself was used to determine

the effect of treatment. Graph V shows that at all yearly observations the D-Thyroxine treated patients exhibited a relatively lower body weight as compared to their initial weight than the placebo treated patients. The difference is statistically significant at a value of $p < 0.05$ at the third and 5th years of treatment.

Clinical Observations

Table IV shows the clinical events that occurred during five years of observation. Nineteen of the 38 placebo treated patients and 20 of the 33 D-Thyroxine treated patients completed five years of follow up without end point events.

Coronary treatment failures occurred in 20 patients. Nineteen were diagnosed as myocardial infarction. Twelve of the myocardial infarctions occurred in the placebo treated patients, 7 in the D-Thyroxine group; an incidence of 27 percent of first reinfarction in the total group (counting dropouts) during the 5 years period. The remaining coronary treatment failure was an episode of prolonged coronary insufficiency, which in the opinion of the authors required that treatment be discontinued. It turned out that the patient was receiving placebo.

There were five cerebrovascular accidents; all occurred in the D-Thyroxine treated group. There were also 3 femoral arterial occlusions, all of them in the D-Thyroxine treated group.

Considered either as a whole or as separate end point categories, there is no significant difference in the inci-

**TABLE IV: EVENTS OBSERVED DURING 5 YEARS OF CLINICAL FOLLOW-UP
IN EUTHYROID CORONARY SUBJECTS TREATED DOUBLE BLIND WITH
D-THYROXINE OR PLACEBO**

FIVE YEARS CLINICAL OBSERVATION			
	PLACEBO 38 PTS.	DT-4 33 PTS.	TOTAL 71 PTS.
A. Total admitted to study	38	33	71
B. Completed 5 years in study	19	20	39
C. Treatment failures	26	22	48
1. Coronary	13	7	20
(a) Reinfarction	12	7	19
(b) Coronary Insufficiency	1	0	1
2. Thrombosis, cerebrovascular	0	5	5
3. Arterial occlusions	0	3	3
D. Deaths	2	5	7
1. Myocardial infarction	2	4	6
2. Other causes	0	1	1
E. Dropouts	6	6	12
1. Moved to the States	2	1	3
2. Incapacity (not able to come)	1	2	3
3. Not interested in treatment	2	2	4
4. Deaths not M. I.	0	1	1
5. M. I. after dropout due to No. 3	1	0	1

dence of thrombotic events between both groups.

There were 7 deaths during the five years of observation. Six were due to myocardial infarction; four in the D-Thyroxine treated group and two in the placebo group. This represents an incidence of 8.5 percent in the total group (counting dropouts) during the 5 years period. There was one other death in the D-Thyroxine treated group due to carcinoma of the pancreas.

Drop out losses due to inability or unwillingness to continue treatment were 6 or 16 percent in the placebo group and 6 or 18 percent in the D-Thyroxine group. The causes for dropout were evenly distributed between both groups and did not appear to be related to the therapy.

Discussion

Serum Cholesterol effects:

Although the observed decrease in the serum cholesterol in the treated group is statistically significant, it is rather small, averaging 12.66 mg.percent below the initial value during the first year, 14.00 mg.percent during the second, 12.75 mg.percent during the third, 18.59 mg.percent during the fourth, and 30.37 mg.percent

during the fifth. There are at least two important reasons for this. First, it must be remembered that due to the overt coronary disease of the subjects, no attempt was made to obtain a maximal effect. Obviously, higher doses of D-Thyroxine would have produced a greater hypocholesterolemic response, but at the risk of a possibly hazardous calorogenic effect. Second, and even more important, is the fact that most of the subjects were normocholesterolemic to start with. We have previously observed that in D-Thyroxine treated patients, the magnitude of the decrease in the serum cholesterol is closely related to the initial level (11). Those patients with initial serum cholesterol levels above the mean for the group showed mean annual decreases of -10.5 percent to -30 percent of baseline while those with an initial level below the mean showed mean annual changes from -13.5 percent to +5 percent of baseline. Thus, if hypercholesterolemic subjects had been selected, the drug would have produced a more pronounced hypocholesterolemic response.

Even though the average decrease in serum cholesterol was small, it should be noted that it was

maintained at substantially the same level throughout the five years of treatment. Thus, the D-Thyroxine treated group as a whole did not exhibit a drug escape effect. The change may be regarded as a significant resetting of the average serum cholesterol at a lower level in the treated patients. This did not occur in the placebo treated patients. However, it should be noted that serum cholesterol decrease did not occur uniformly and consistently in all actively treated patients. At any one time only about 2/3 of them showed a decrease. In general, patients with the higher initial cholesterol levels tended to keep their cholesterol decreased more consistently over the years than those with the lower initial levels. This observation again reflects the greater effectiveness of the drug in those patients with the higher initial serum cholesterol.

In the relatively small number of patients of the present study, the initial serum cholesterol was not predictive of the occurrence of new infarction. Those patients of both groups who developed new infarctions had an average initial serum cholesterol of 202.1 mg. percent which is not significantly different from the initial overall average for all patients. If we had tried, we would not have been successful in selecting for treatment on the basis of the serum cholesterol those patients who were going to develop new infarctions. Of course, this is to be expected in a relatively small group of patients who do not exhibit marked deviations from the normal in their serum cholesterol. From the practical standpoint, this raises the question of how effective minor decreases of the serum cholesterol would be in such patients in terms of decreasing their reinfarction risk.

Some investigators (18) have noted a seasonal variation in serum cholesterol in normal subjects. The data of the placebo treated group were distributed in seasonal trimesters and studied according to the analysis of variance. The highest values in serum cholesterol were noted from October to December and the lowest from July to September. However, according to the technique of analysis of variance, there was no significant seasonal difference in our placebo treated subjects.

B-Lipoprotein effects:

In general, the changes in serum beta lipoprotein due to D-Thyroxine followed closely the pattern of changes in the serum cholesterol. The average beta-lipoprotein value was significantly lower at every yearly observation in the D-Thyroxine treated group. As with the serum cholesterol the decrease in beta-lipoprotein was significantly more marked, uniform, and constant in those patients with the higher initial levels of serum beta-

lipoprotein. It may be stated that in the D-Thyroxine treated group there was a significant resetting of the mean beta-lipoprotein at a level lower than the initial value. This resetting was not observed in the placebo treated group.

The average initial beta-lipoprotein level of those patients who subsequently developed a myocardial infarction was not significantly different from the level of those who did not. Therefore, the beta-lipoprotein value, like the serum cholesterol, was not predictive for the complication of repeat myocardial infarction in this study.

Other biochemical effects:

An increase in RBC - T_3 uptake and a decrease in I 131 thyroid uptake was characteristic of patients receiving D-Thyroxine throughout the five years of observation. These changes were so consistent that they enabled an independent third party to confirm to the investigators that the patients were actually taking the medications as prescribed. The decrease in I 131 uptake is consistent with thyroid iodine uptake suppression caused by D-Thyroxine. It has been reported that regardless of its iodine content, D-Thyroxine at dosage levels less than 6 mg. per day suppresses thyroid iodine uptake in euthyroid subjects while it fails to suppress it in hyperthyroid subjects (19). The increase in RBC - T_3 uptake is consistent with occupation of binding sites at the RBC membrane by D-Thyroxine.

As was noted under "Results", there were no significant differences between active and placebo treated patients in the other laboratory determinations made.

The observations do not substantiate any evidence of either hepatic, renal or hematologic toxicity of the drug.

Side Effects:

As judged by the severity, increased frequency and the duration of pre-existing angina, D-Thyroxine produced a calorogenic effect in the treated patients of the present series. In the original design of the study, it was planned to observe the effect of increasing the dosage of some patients to 6 or 8 mgs. per day. However, when a preliminary examination of the data indicated that there was a worsening of pre-existing angina, the attempt was abandoned. It is believed that preexisting angina represents a limiting factor regarding the maximum dosage of D-Thyroxine in these patients. However, it should be emphasized that the investigators were quite sensitive to the possible angular hazard of the drug and that changes in the angular pattern of the patients were specifically sought for.

Actually, the worsening of angina was not considered to be an indication for discontinuation of treatment except in the one patient who developed a prolonged state of coronary insufficiency. It turned out that he was receiving a placebo rather than the active drug. It is believed that under judicious observation the dosage of 4 mg per day of D-Thyroxine is well tolerated by selected patients with evidence of coronary artery disease, including moderate degrees of stable angina pectoris.

It is of considerable interest that new angina during the period of observation developed in even more patients of the placebo group than of the D-Thyroxine group: 8 versus 3 patients respectively. The incidence of complaints related to the severity and frequency of anginal episodes in these patients was not significantly different between both groups. However, the number of patients in this subgroup is too small to permit definite conclusions. It appears that at the dosage level used in the present study, D-Thyroxine did not introduce a significant predisposition to new angina.

Other calorogenic side effects attributed to D-Thyroxine were not identified except for a relatively lower body weight and a higher tendency to diarrhea in the treated group. Tachycardia, palpitations and nervousness were not significantly different in both groups. Both weight loss and diarrhea were relatively minor, but in the patients who developed them, they tended to be constant throughout the period of therapy as long as treatment was continued. The patients did not object remarkably to the increase in frequency of bowel movements and at no time did these symptoms necessitate discontinuation of treatment.

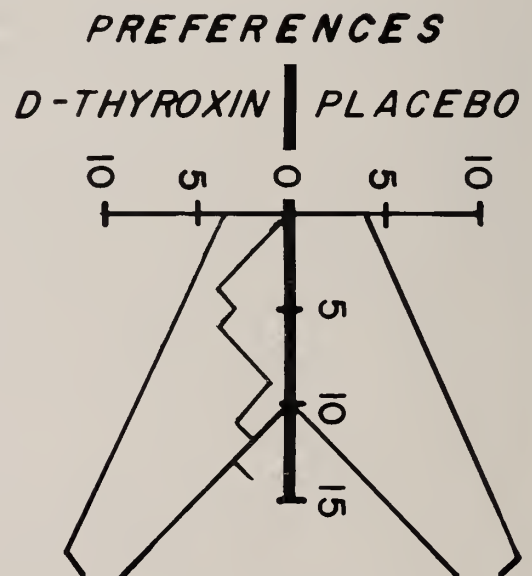
Effects on reinfarction and mortality:

As previously described, 19 reinfarctions and one episode of prolonged coronary insufficiency occurred during the period of the study. This number includes only first events since once a patient developed an event he was taken off double blind treatment. As previously noted, the chance of developing an event was apparently not related to a higher initial serum cholesterol or beta-lipoprotein level. No significant relationship was found between the subsequent development of a coronary event and either hypertension, age, fasting blood sugar, preexisting angina, previous myocardial infarction, smoking, weight or serum uric acid.

According to the planned design of the study, the patients were paired sequentially in order of randomization into either the placebo or the D-Thyroxine treated group according to the sequential analysis technique described by Armitage (20). Preferences for one or the

other regime were established on the basis of the length of time under treatment that it took for the event to occur. The preferences were entered into a sequential design selected so as to enable a decision with a maximum of 19 preferences as shown in graph VI. At the time that the study was planned it was anticipated that this number of preferences could be reasonably expected to occur in 71 patients within a five year period. Crossing of either the upper or the lower margin of this diagram would be due to chance less than one time in twenty ($p < .05$). The design has a 95 percent power of detecting a true preference ratio of 9:1.

At the end of five years of observations 14 preferences were established, 8 favoring D-Thyroxine, and six favoring the placebo. Patient pairs in which one of the partners dropped out before reaching end points were excluded. It may be seen that the lateral boundary of no decision was crossed which indicates that a critical preference ratio of 9 to 1 is not present. It is entirely possible that a real preference may exist, but at a ratio such as to require a greater number of preferences in order to be detected. For example, according to Armitage (20), a sequential design that would have a 95 percent power of detecting a real preference ratio of .55 to .45 could require a maximum of 1778 preferences. The present study does not supply any statistically significant data to anticipate that an experiment of this



size would or would not demonstrate significant results. Therefore, the question awaits completion of suitable larger scale prospective studies.

It must be emphasized that this study was planned to determine the value of hypocholesterolemic therapy under the least favorable circumstances. It is true that in usual practice, the patient who already has had a myocardial infarction would be the one to come most frequently under consideration for this form of treatment. However, it must be realized that at this stage, the disease is already far advanced and has led to changes of questionable reversibility. Another point is that if one or several predisposing factors of atherosclerosis are to be picked out for control, they should be the ones showing the most definitive abnormality. There is evidence already that probably hypercholesterolemic subjects can be benefited through hypocholesterolemic therapy from the standpoint of atherosclerotic complications (9, 10). Certainly, subjects with mild hypercholesterolemia would be least apt to benefit from hypocholesterolemic therapy, no matter how effective the latter might be.

Since the consideration of hypocholesterolemic therapy is going to keep coming up in the practical clinical situation, the importance of determining its effectiveness under the circumstances described remains valid. It would seem that the first objective of the present study regarding the feasibility of hypocholesterolemic therapy with D-Thyroxine in coronary subjects can be answered tentatively in the affirmative for the experimental situation if small doses are employed and the necessary precautions taken. The second objective which considered the long term tolerance of the drug from a calorogenic standpoint can also be answered affirmatively if one is ready to accept that the effectiveness of the hypocholesterolemic response must be tempered according to the calorogenic effects. Doses of D-Thyroxine larger than 4 mg. per day do not seem to be well tolerated by most of these patients. The third objective regarding the effect on the morbidity and mortality of the disease in this type of patients has not been answered by the present study. However, it appears more approachable after it is established that these patients can tolerate this form of therapy without serious adverse effects. The findings would allow a trial under controlled experimental circumstances on a larger number of individuals in whom a beneficial effect might be revealed. It would seem logical to concentrate such a trial in situations where differences would be more clearly discernible such as those subjects with frank hypercholesterolemia

without predominance of other high coronary risk factors. Therefore, the effectiveness of hypocholesterolemic therapy with D-Thyroxine in known coronary subjects remains a problem to be elucidated through additional investigations.

Summary

Seventy one patients who had sustained one or more definite myocardial infarctions were given daily either 4 mg. of D-Thyroxine (DT₄) or its placebo. A double blind envelope design was used. Thirty eight patients were assigned to the placebo regime and thirty three to the DT₄ regime. All patients reached either a terminating event or completed five years of treatment. There were 20 coronary treatment failures: 13 in the placebo treated group and 7 in the D-Thyroxine treated group. There were 4 deaths due to repeat myocardial infarction in the D-Thyroxine treated group and 2 in the placebo treated group. Dropout losses were approximately the same in both groups. In spite of a greater severity, increased duration and higher frequency of preexisting angina, and a higher frequency of diarrhea in the D-Thyroxine treated group, the drug was well tolerated and did not have to be discontinued because of side effects in any patient. The drug produced a significant decrease in serum cholesterol, a decrease in Beta-lipoproteins, decrease in thyroidal I 131 uptake and an increase in triiodothyronine (T₃) RBC uptake. It did not affect significantly the morbidity or mortality of the treated group during the duration of the study.

Conclusions

1. D-Thyroxine is an effective hypocholesterolemic agent in euthyroid coronary subjects; the hypocholesterolemic effect is more marked the higher the initial cholesterol value.

2. At a dosage level of 4 mg. per day this drug produced a mild but significant calorogenic effect on patients who had sustained a myocardial infarction. This was manifested by a significant increase in frequency, severity, and duration of preexisting angina, a significant increase in diarrhea, and a significant body weight limiting effect. The drug did not induce significantly new angina or other calorogenic effects in these patients.

3. At the dose level specified, the side effects were not serious and did not necessitate discontinuation of

treatment in any patient.

4. The occurrence of 20 end point events and the establishment of 14 preferences during five years of continuous observation of the 71 subjects of this experiment did not enable the detection of either a beneficial or a harmful effect of this therapy on the morbidity or mortality of coronary artery disease.

5. The present findings would be consistent with the continuation of controlled experimental trials on a larger numbers of carefully selected subjects in which a beneficial effect of this form of treatment might be identified.

Resumen

Setentiún pacientes que habían sufrido uno o más infartos del miocardio definitivamente comprobados recibieron 4 mg. de D-Thyroxine o su placebo. Treinta y ocho pacientes fueron asignados al azar al tratamiento con placebo y 33 al tratamiento con D-Thyroxine. Todos los pacientes llegaron a un evento terminante o completaron 5 años de tratamiento. Veinte tuvieron un evento terminante: 13 del grupo tratado con placebo y 7 del grupo tratado con D-Thyroxine. Ocurrieron 4 muertes debido a infarto del miocardio en el grupo tratado activamente y 2 en el grupo de placebo. El número de pacientes que se retiraron del estudio por causas fortuitas fue aproximadamente el mismo en ambos grupos. A pesar de que la angina presente antes del tratamiento se empeoró significativamente en severidad, duración y frecuencia de los episodios, y de una frecuencia más alta de diarrea, los pacientes tratados con D-Thyroxina toleraron bien la droga. Esta no tuvo que ser descontinuada por efectos secundarios en ningún paciente. La droga produjo un descenso significativo en el colesterol sérico, en el nivel de Beta-lipoproteína, y en la captación de yodo radioactivo por la tiroide, y un aumento en la captación de tri-iodo-tironina por la células rojas en los pacientes tratados activamente. La D-Thyroxine no afectó significativamente la morbilidad y mortalidad del grupo tratado durante la duración del estudio.

Acknowledgment

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EN TORNO A LA FIEBRE REUMATICA

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La fiebre reumática es una enfermedad del tejido conjuntivo que surge como consecuencia de una infección estreptocócica. Se presenta al desarrollarse una reacción antigénica a esta bacteria, después de un período de latencia de aproximadamente dos semanas, manifestándose en múltiples órganos y tejidos. Los efectos en las articulaciones (artritis migratoria), la piel (eritema anular), el tejido subcutáneo (nódulos), y el sistema nervioso central (corea de Sydenham) son reversibles, no así los efectos en el corazón (pancarditis). Esta enfermedad afecta principalmente a los niños de edad escolar, entre los 7 y los 15 años (1).

El ataque inicial representa el 85 por ciento (2) del total de casos diagnosticados. La enfermedad se caracteriza por recurrencias al producirse una re-infección con el estreptococo, siendo los ataques repetidos más nocivos que el inicial.

La fiebre reumática hace sus efectos en el sistema cardiovascular durante la fase aguda, pero la severidad de la incapacidad se hace evidente 10 a 30 años después del ataque inicial. Esto afecta a la fracción más productiva de la población, con las consecuencias que esto acarrea para la sociedad en general.

En Puerto Rico, la enfermedad cardíaca causada por la fiebre reumática representa el 12.2 por ciento del total de enfermedades cardiovasculares informadas al Departamento de Salud *. Aunque tenemos a nuestro alcance los medios para erradicar esta enfermedad, identificando el estreptococo Beta hemolítico e instituyendo un tratamiento precoz, si comparamos su incidencia actual con la de los años '30 vemos que ha disminuído sólo en un 30 por ciento (2). Aunque la mortalidad del ataque inicial es relativamente baja, la morbilidad es significativa, aumentando progresiva-

mente con el pasar de los años, según la dinámica cardiovascular cede a la sobrecarga crónica. Es, pues, más juicioso, y mejor inversión, el prevenir esta enfermedad, concentrando nuestros esfuerzos en disminuir la incidencia de infecciones estreptocócicas y evitando recaídas en los pacientes afectados.

El programa para la prevención de la fiebre reumática que se ha emprendido con fondos federales (Médico Regional), estatales (Departamento de Salud), municipales (Programa de Ciudad Modelo), locales voluntarios (Asociación Puertorriqueña del Corazón) y que dirige la Escuela de Medicina a través de la sección de Cardiología Pediátrica del Hospital Universitario se ha dividido en dos grandes fases:

1. Prevención primaria
2. Prevención secundaria

PREVENCIÓN PRIMARIA:

La prevención primaria se logra con la detección correcta y temprana de la infección estreptocócica y con su tratamiento adecuado. Para hacer el diagnóstico correcto de una faringitis por estreptococo es necesario el examen clínico y de laboratorio.

Es de fundamental importancia establecer el diagnóstico con un cultivo de garganta. Por lo tanto, el médico necesita un laboratorio rápido y eficiente, que esté equipado para identificar el organismo y para determinar su grupo serológico.

A todo paciente que presente el síndrome de faringitis de origen súbito, fiebre, dolor de cabeza, dolor al tragar, una garganta roja, hinchada, con exudado y petequias, y con glándulas cervicales dolorosas, se le debe tomar muestra para cultivo de garganta. Este "cuadro típico" puede ser causado por infecciones virales, como también puede una infección estreptocócica producir síntomas mucho menos dramáticos y pasar desapercibida. No obstante el cuadro clínico, el 3 por ciento (2) de todas las infecciones por estreptococo son seguidas de Fiebre Reumática. Si no hay disponible las facilidades de cultivo, se debe tratar al paciente en cuanto se haga clínicamente el diagnóstico. Es también recomendable tomar muestras para cultivo a los contactos

* - *Análisis de la experiencia de The Heart Disease Control Program, clínicas durante el período de Julio 1, 1962 a Junio 30, 1967.*

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de pacientes positivos.

El método de laboratorio a usarse debe ser rápido y económico. Muchos laboratorios identifican todos los organismos en un cultivo de garganta y determinan la sensibilidad a varios antibióticos. Esto es costoso y no es necesario. La identificación de otros organismos, muchas veces no patógenos, no tiene ningún valor y el estreptococo es todavía sensible a la penicilina.

Ya que las infecciones por estreptococo afectan mayormente a nuestros niños, el programa de prevención en Puerto Rico se ha iniciado en las escuelas elementales. Se adiestra a los maestros en la toma de cultivos y en la inspección de la garganta del niño enfermo. El programa provee a las escuelas el material necesario para la toma y envío de cultivos. También se ha implicado al dentista en la detección y la toma de cultivos, ya que ellos ven con frecuencia a pacientes enfermos que desatienden el consultar a un médico para "un dolor de garganta". El programa se ha establecido en Barranquitas y en áreas de San Juan.

El laboratorio del programa usa la técnica de la fluoresceína, haciendo posible una identificación rápida. Los organismos aislados son clasificados según su tipo serológico, en caso de encontrar una incidencia alta en algún sector (sobre 10 por ciento). El laboratorio está al servicio de todos los médicos y dentistas que quieran participar en el programa de prevención y proveerá material de cultivo, así como los medios de envío de muestras. Los resultados llegarán al médico dentro de las 24 a 48 horas subsiguientes. Se estimula que se usen estas facilidades a su capacidad máxima.

El tratamiento ideal para una faringitis estreptocócica es la penicilina benzatínica (3) *. Con una sola dosis de larga duración está el paciente adecuadamente tratado **. Una vez se decida tratar una faringitis, el tratamiento debe encaminarse a la erradicación del estreptococo y la prevención de la fiebre reumática.

¿Cuál es el riesgo que tienen nuestros niños de escuela elemental de desarrollar fiebre reumática?

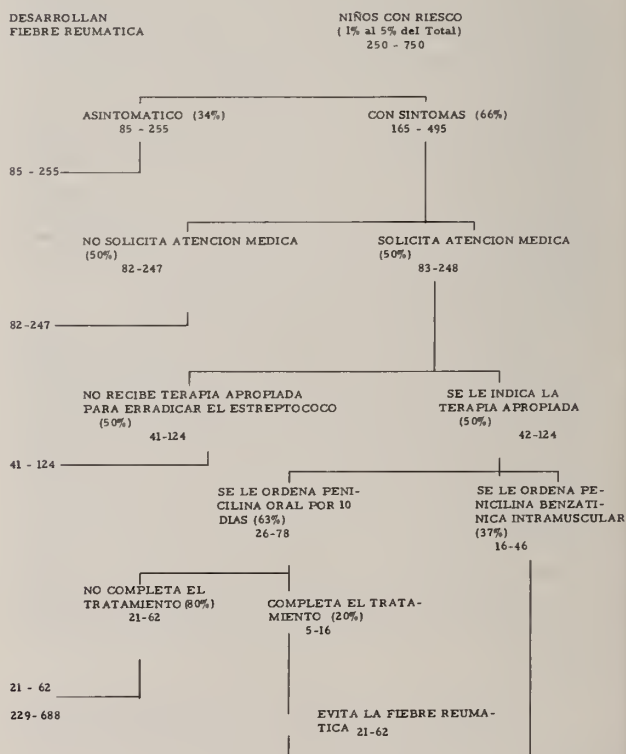
La matrícula de las escuelas elementales públicas de Puerto Rico es de aproximadamente 500,000 niños. * En este grupo de niños, la incidencia de infección por estreptococo beta hemolítico fluctúa entre 5 a 10 por ciento; en ocasiones ha llegado a un 41 por ciento. ** Conservadoramente podemos resumir que hay en Puerto Rico 25,000 niños portadores de esta bacteria.

De éstos, del 1 al 3 por ciento desarrollan fiebre reumática (250-750 casos) primaria, si no erradicamos el estreptococo beta hemolítico a tiempo.

¿Qué sucede con este grupo de alto riesgo?

Aplicando la tabla esquemática diseñada por Perry y Henikoff (4) podríamos proyectar el futuro de estos niños en la siguiente forma:

TABLA ESQUEMATICA



* - Penicilina benzatínica (benzetacil), 600,000 unidades IM para niños de menos de 60 libras y 1,200,00 unidades IM para niños mayores. Si el paciente es alérgico a la penicilina, deberá usar eritromicina, 50 mg./kg./día por diez días.

** - Se ha demostrado que el 80 por ciento de los pacientes no terminan el tratamiento de diez días si éste se prescribe por vía oral.

* - 1967 - Grados comprendidos de Kindergarten a sexto grado.

** - Estudio realizado en 1971.

De los 250-750 niños que tienen un alto riesgo de desarrollar fiebre reumática, solamente 165-495 notarán síntomas de la infección estreptocócica. De éstos, la mitad, (83-248) solicitarán ser vistos por el médico, el cual la identificará y prescribirá la terapia bactericida en 50 por ciento de los casos (42-124). Sesentitrés por ciento de éstos (26-78) recibirán orden de terapia oral adecuada (por diez días), pero el 80 por ciento de ellos (21-62) no la terminará. Evitarán la enfermedad los 16-46 casos que recibieron terapia con una sola inyección de la penicilina benzatínica y el 20 por ciento (5-16) que completó la terapia oral, evitándose la fiebre reumática en sólo 21-62 de los casos (8.4 por ciento).

El programa intenta:

Llevar el tratamiento al grupo sintomático (66 por ciento) y recultivar al terminar la terapia, para determinar si hubo re-infección. Hemos encontrado un 5 por ciento de re-infección. El estudio de estos pacientes nos ayuda a identificar los casos asintomáticos.

PREVENCION SECUNDARIA:

La fase de prevención secundaria es de suma importancia, ya que el paciente que ha tenido el primer ataque de fiebre reumática es más susceptible a un segundo ataque que usualmente es tan grave, que amenaza de muerte al paciente.

La penicilina benzatínica (Benzetacil 1,200,00 unidades) intramuscular cada 28 días es la profilaxis indicada. Se conoce que los pacientes mantienen su profilaxis más fácilmente con una inyección cada 4 semanas que por vía oral. Los que son alérgicos a la penicilina deben usar sulfadiazina, un gramo diario.

Se ha descubierto en Barranquitas a 33 pacientes con historial de fiebre reumática, de 3,000 niños estudiados en 14 escuelas elementales. Estos niños han sido integrados al programa de profilaxis. Se proyecta establecer centros de profilaxis a través de toda la isla. Estos centros estarán dirigidos por personal local, todos bajo la supervisión del programa central.

Para tener control óptimo de los pacientes, y como ayuda en su seguimiento, se desarrolló en Barranquitas un registro de pacientes. Este registro incluye a todos los pacientes de fiebre reumática del área. Con el registro, se dispone fácilmente de información sobre todos los pacientes que reciben profilaxis y es posible vigilar su seguimiento. Toda la información de los registros locales se tiene en el registro central del programa. El registro central debe incluir los que pertenecen a programas ya establecidos, los pacientes de médicos privados y hospitales privados y públicos. Este debe

proveer data de validez estadística, debe ser flexible y fácil de manejar, debe tener a la mano la información sobre pacientes participantes.

El seguimiento de los pacientes se debe hacer con la ayuda del programa de prevención, utilizando el laboratorio y todos los servicios que se proporcionen en el mismo. Solamente de esta manera se asegura la efectividad de éste.

La sección de Cardiología Pediátrica del Hospital Universitario ofrece servicios de consulta médica, consejo social y de rehabilitación a todos los pacientes que participan en el programa. También se ha establecido un campamento de verano para niños que han tenido fiebre reumática. En el campamento hay actividades recreativas a la vez que se enseña a los niños y sus padres los fundamentos básicos de la enfermedad que les afecta y la importancia de la profilaxis. Se pondera lo psicológico y lo social de estos niños durante su estancia en el campamento. Hemos encontrado que gran parte de ellos presentan problemas psicológicos serios, * secundarios a su enfermedad. Si éstos permanecen sin diagnóstico y tratamiento temprano terminan por incrementar la incapacidad del paciente.

Para que un programa de prevención amplio funcione efectivamente, es necesario crear un comité central que organice y dirija las actividades. Este comité debe estar integrado por personas interesadas en el problema, e incluir médicos, dentistas, administradores, profesionales activos en los servicios de salud, educadores y otros líderes de la comunidad. Los médicos miembros del comité deben estar al tanto de los problemas de salud de la comunidad.

Como paso inicial, el comité debe estimar la incidencia y magnitud del problema. Esta información se puede obtener con la cooperación de hospitales públicos y privados, médicos privados que reporten la enfermedad, pacientes que se descubran en encuestas y en oficinas de reclutamiento de las fuerzas armadas.

Es responsabilidad del Comité de Fiebre Reumática el educar a los médicos, estudiantes de medicina, enfermeras, y otros profesionales en la bacteriología del estreptococo y su relación con la fiebre reumática. Los médicos participantes en el programa se deben mantener informados de todos los adelantos y descubrimientos en la profilaxis y el tratamiento. Toca al comité, no solamente dar estos servicios sino, además, fomentar el estudio de, y la investigación sobre,

* - Comunicación personal - Dra. L. M. Guevara, Siquiatra pediátrica.

la enfermedad. La creación de este comité es uno de nuestros objetivos para el próximo año.

Es necesario evaluar el programa de prevención. Para ello, resulta valioso el asesoramiento de un epidemiólogo. El propósito del programa no es sólo combatir efectivamente la enfermedad, sino también establecer criterios y datos de valor estadístico de la enfermedad en el área. Esto conduce a un mejor entendimiento del comportamiento del estreptococo en la población estudiada y a un mejor manejo de los pacientes afectados.

Como creemos que es de suma importancia que el pueblo esté informado de estos programas para que los servicios sean utilizados plenamente, se comenzó una campaña de educación al pueblo, usando la televisión y otros medios de comunicación para difundir la información.

Los esfuerzos iniciales de la Sección de Cardiología Pediátrica del Hospital Universitario van encaminados a la prevención de la fiebre reumática en Puerto Rico. Esta meta se logrará solamente con el apoyo de la comunidad en general y la participación amplia de todos aquellos envueltos en el cuidado de pacientes.

Resumen

Se discuten las recomendaciones para establecer un programa de prevención primaria y secundaria de fiebre reumática. Se ilustran estas recomendaciones con el programa que se está desarrollando en Puerto Rico.

Summary

The recommendations for instituting adequate primary and secondary prevention programs for Rheumatic Fever are discussed. These points are illustrated with the program being established at the present time in Puerto Rico.

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THE TOXICOLOGY OF ASPIRIN

Sidney Kaye, MSc, PhD

If ever a drug deserves to be called a "Wonder Drug", it is aspirin. What single drug known to man has been used so widely with such wonderful results and for so many years, (since 1899)? Its annual consumption far exceeds all other drugs, (22,000 tons were used in 1970 in the United States).

Aspirin is still one of the best antipyretic, antirheumatic and analgesics providing much benefit with little risk. For the adult there is a wide margin of safety. The approximate minimum lethal dose (MLD) for a man (150 lbs) is about 15 gms which represents 45 (5 grain) adult tablets. For this reason we see so few accidents or successful suicides involving aspirin in adults.

On the other hand aspirin is the number one killer for children in the United States. More children between the ages of 1 and 6, die each year from aspirin than from any other single poison. Children under 3 are very susceptible, perhaps due to a specific enzyme lack. Fever and convulsions are more common in infants who usually die in renal failure or cardiovascular collapse while in coma.

Perhaps the high incidence of mortality in children is due in part to a sense of security we have toward the use of aspirin. It is used so freely and so often. It works so well and is found in abundance in everyone's home. How then can anything so common and so safe be so deadly?

Overdosage

Overdoses in children occur in several ways:

1. An overzealous mother treating a sick or feverish infant, (or young child).
2. A mother coaxing her child to take his "flavored" aspirin by calling it "candy", and is later shocked to find the bottle empty: the child believed his mother.

3. Children playing doctor, nurse, and patient with aspirins.

Aspirin poisoning in a child is especially dangerous since the child does not always appear to be very ill in the early stages. "If only it could have been recognized before most of it had been absorbed!"

As early recognition and prompt treatment can often make the difference between survival and death or could at least minimize residual damages, the following resumé is offered:

Acetyl Salicylic Acid



Synonyms: Aspirin: M.P. 137° C; MLD approximately 15 gm/150 lb. man.

Derivatives: Sodium salicylate, MLD approximately 15 gm; phenyl salicylate (salol), MLD 5 gms., M.P. 42° C.; Methyl salicylate (oil of wintergreen), MLD 10 ml; salicylic acid, MLD 5 gms., M.P. 157° C.

Uses: Analgesic, antipyretic, antirheumatic.

Properties: Odorless, bitter tasting, white crystalline; soluble in ethanol, chloroform or ether.

Remarks: Salicylates are rapidly absorbed, can usually be detected in the urine within 30 minutes, and have a long half life of about 24 hours. As little as a 0.3 gms. tablet will give a positive test in the urine. Allergy is not common but local irritation and gastrointestinal bleeding may be produced by most salicylates. This is minimized with food or liquids (milk).

Symptoms: The most serious symptom is the metabolic acidosis that is produced, but this is a delayed effect. Nausea and vomiting may occur early or may also be delayed. Large doses of aspirin may first stimulate and then depress the central nervous system; initial excitement and convulsions may be followed by stupor and depression. Central nervous stimulation may also produce hyperventilation (loss of CO₂), and early transient respiratory alkalosis. However, this is followed by a severe metabolic

acidosis. Other possible manifestations are: Headache, dizziness, cyanosis, para-amino phenol in urine (brown-black urine), diaphoresis, sugar in the urine, thirst, gastritis with or without gastric hemorrhage, prolonged prothrombin time, bleeding gums, disturbance of hearing and vision, tinnitus, peripheral vaso-dilation, hyperpnea with dyspnea, weakness and fatigue, hypotension, irritability, delirium, confusion, renal and brain damage, respiratory failure, collapse, coma, death.

Identification: Separated by acid-ether extraction. Specimen must be strongly acid to allow a good extraction.

Tests

1. To 5 ml of urine, add 1 ml of 10 percent ferric chloride and heat gently to rule out possible false reaction due to acetone bodies. If salicylate is present, a purple color will persist. This test is very sensitive and is positive in urine even after the ingestion of one 0.3 gm aspirin tablet, but is also positive for sodium, phenyl, or methyl salicylates, and other phenol derivatives.

2. Acidify 5 ml of blood by adding 0.5 ml of 2N hydrochloric acid. Then extract with 10 ml of ethylene dichloride, allow layers to settle and separate. Discard upper blood layer, and add 2 ml of 0.2 percent ferric nitrate to the ethylene dichloride. A purple color, produced if salicylate is present, can be compared with standards similarly prepared.

3. (Natlson)

(a). 0.1 ml of serum or urine is put on a white porcelain dish and then 1 drop 1 percent nitrate (in 0.07 N HNO_3) is added. A purple color is positive for salicylates and results are reported as negative, faint, moderate or large amounts.

(b). Quantitative:

0.2 ml serum or urine plus 0.8 ml of water is measured into each of two small test tubes. To one T. T. (which will be the blank) add 1 ml of 0.07N nitric acid. To the other (which will be the unknown) add 1 ml of 1 percent $\text{Fe}(\text{NO}_3)_3$. Mix and allow to stand for about 5 minutes, and then read in a spectrophotometer at 540 nm.

For standard: Put 1 ml of H_2O in 1 T.T. (blank) and then add 1 ml of 0.07N HNO_3 : To another T.T. add 0.8 ml of water and 0.2 ml of standard and then 1 ml of 1 percent $\text{Fe}(\text{NO}_3)_3$.

$$\frac{\text{Absorbance unknown}}{\text{Absorbance standard}} \times 25 = \text{mg salicylate/100 ml}$$

Remarks

Results are reported as negative, small, moderate or large amounts, as compared with standards. Blood levels above 20 mg percent may be toxic; lower levels may be toxic to infants who have been known to be "over treated" by over zealous mothers. The finding of salicylates in the blood or urine, in itself is of no great emergency, unless the level is high. In all questions of doubt, there should be a determination of the alkali reserve of blood. It is of utmost importance to determine the degree (if any) of acidosis. The simple FeCl_3 test is of great help, whenever there is a doubt of intake. Children may sometimes have a delayed response, and appear to be in better condition than they actually are. This test can alert the physician to immediate action.

Treatment

Gastric lavage with water, or syrup of Ipecac to induce vomiting are recommended. Do not omit lavage or emesis unless dose is known to be small, or exposure was more than eight hours ago. Patient may appear deceptively well when first seen for signs and symptoms such as vomiting may be delayed several hours.

Oral or parenteral fluids will increase urinary output, and will counteract dehydration due to vomiting and sweating. Maintain body heat, fluids and electrolyte balance; keep patient warm and quiet, and give alkaline drinks.

Sodium bicarbonate or sodium lactate M/6 IV, to combat acidosis and sodium loss are prescribed if necessary. Periodic blood determinations for alkaline reserve will estimate severity of poisoning, and progress of treatment. Recovery may depend upon renal elimination and correcting acidosis. Elimination of salicylate is more rapid if urine is kept alkaline.

Vitamin K derivatives and Vitamin C may be given to counteract a prolonged prothrombin time and increased capillary fragility, respectively.

In severe poisoning, an exchange transfusion or hemodialysis (artificial kidney) may prove helpful.

Sedation for restlessness is helpful, but morphine derivatives are contraindicated. Oxygen and artificial respiration may be needed to support respiration.

Summary

Aspirin has been the most frequent poisoning and killer of children in the United States for many years. This has not been so in Puerto Rico. However, within recent years, more and more cases of aspirin poison-

ing in children have been occurring.

The test for detecting an overdose of aspirin is very simple and can be performed by anyone, anywhere. The negative "Ferric Chloride" test is very definite and specific; and a positive test is surely strongly presumptive especially with a good history and typical signs and symptoms.

Much depends upon a reliable, rapid diagnosis and prompt initiation of treatment, as specific and effective treatment is available.

Resumen

Por muchos años, la aspirina ha sido responsable del mayor número de muertes y de envenenamientos en niños en los Estados Unidos. Este no ha sido el caso en Puerto Rico, aunque sin embargo, cada vez con mayor frecuencia se registran casos de intoxicación con as-

pirina en Puerto Rico.

El análisis para la detección de una sobredosis de aspirina es muy sencillo y fácil de hacer por cualquier persona, en cualquier parte. La prueba negativa del "Cloruro Férrico" es muy específica y definitiva, a la vez que un resultado positivo es, aunque de naturaleza preliminar, altamente indicativo de intoxicación especialmente en presencia de un buen historial y de señas y síntomas típicos.

Un diagnóstico rápido es de gran importancia ya que existe un tratamiento específico para dichas intoxicaciones.

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EFFECTIVENESS OF MINOCYCLINE IN BACTERIAL INFECTION

Lillian Conde Pérez, MD

Minocycline base is a yellow crystalline powder, a semisynthetic derivative of the tetracycline family. Its antibacterial spectrum is greater than that of the other tetracyclines, being effective against gram negative as well as gram positive bacteria (1). It is unique among tetracyclines because of its effectiveness against tetracycline sensitive staphylococcus aureus as well as against tetracycline resistant staphylococcus aureus (2, 3). Bacterial resistance to Minocycline may develop slowly in a stepwise fashion and apparently in a lower order of magnitude than resistance to other tetracyclines (3).

This study was undertaken to corroborate the effectiveness of Minocycline in gram negative as well as gram positive bacterial infection and in staphylococcus aureus infections.

Material and Methods

Fifty three patients with different types of infections were treated with Minocycline in an eight-month period at the Medical Department, San Juan City Hospital and Emergency Room, Puerto Rico Medical Center. None of the patients had septicemia. Two-hundred milligrams of Minocycline were given orally as a loading dose followed by one-hundred milligrams each twelve hours. Treatment was given for a total of ten days in the majority of cases due to the severity of the infection. The antibiotic was not tested in children nor pregnant women.

A complete blood count, urinalysis, fasting blood sugar, blood urea nitrogen, serum glutamic oxalacetic transaminase, serum glutamic pyruvic transaminase and serum lactic dehydrogenase were done before starting treatment, on the fifth to seventh day of treatment, and three to four days after finishing treatment.

Culture and sensitivity studies of the infecting organism and renographic studies were done before starting treatment, on the fifth to seventh day of treatment and three to four days after discontinuing therapy. It was our interest to detect any change in kidney function during Minocycline therapy

Results

A total of fifty three patients received Minocycline therapy for bacterial infections. One patient discontinued the medication because infection was not found, the second patient discontinued treatment on his own, and the third one discontinued treatment because of severe dizziness. This report comprises a total of fifty patients that completed treatment.

In twenty two patients, the infection was complicating another illness like diabetes, leukemia, congestive heart failure, etc. In twenty-eight cases the infection was the only problem in the patient.

Forty five of the fifty patients showed good response to treatment, that is, they improved clinically and their cultures became negative after cessation of therapy. One patient showed marked clinical improvement but her culture remained positive after discontinuing the treatment. Four patients did not show any improvement and their culture persisted positive but no new organism were cultured from them. The following were the infections that responded to treatment:

<u>INFECTION</u>	<u>NUMBER OF PATIENTS</u>
Urinary Tract Infection	21
Bronchopneumonia	6
Infection of Skin	5
a- Abscesses	2
b- Impetigo	1
c- Infected dermatitis-cellulitis	1
d- Pustules	
Acute Bronchitis	5
Acute Otitis Media	2
Tonsillitis	2
Pelvic Inflammatory Disease	1
Acute Cholecystitis	1
Mastitis	1
Sinusitis	1

Among the patients that responded well to treatment, eighteen had mixed infection, that is, more than one organism was cultured at the site of infection and twenty-seven patients had only one organism at the site infection. The organisms cultured in these patients were the following:

This study was carried out through a grant from Lederle Laboratories, Division of Cyanamid Borinquen.

TABLE I: ORGANISM CULTURED, SENSITIVITY AND RESPONSE TO MINOCYCLINE
IN PATIENTS WITH URINARY TRACT INFECTION

Organism Cultured	Time Cultured	Sensitive to Minocycline by In Vitro Studies	Resistant	Response to Treatment	
				Good	Poor
E. Coli	14	12	2	12	2
Klebsiella	6	5	1	6	0
Pseudomona areuginosa	3	2	1	3	0
Paracolon	3	3	0	3	0
Proteus	3	2	1	2	1
Beta hemolytic enterococcus	2	1	1	1	1
Non hemolytic streptococcus	1	1	0	1	0
Enterococcus	3	2	1	2	1

ORGANISM	INSTANCES CULTURED
Escherichia coli	17
Staphylococcus aureus coagulase positive	11
Pseudomonas areuginosa	8
Alpha streptococcus viridans	6
Klebsiella pneumonia	6
Pneumococcus	4
Beta hemolytic streptococcus	4
Proteus vulgaris	3
Paracolon aerobacter	3
Alpha enterococcus	3
Paracolon klebsiella	2
Beta hemolytic enterococcus	2
Non hemolytic enterococcus	1
Alkaligenes fecalis	1
Intermediate coliform	1
Non hemolytic streptococcus	1
Neisseria-not identified	1
Bacillus subtilis	1

Twenty three patients had urinary tract infections and only two responded poorly to treatment. Thirteen of them had a single organism while ten had a mixed flora in their urine cultured. Most of the organisms were sensitive to Minocycline by in vitro studies.

Staphylococcus aureus coagulase positive was cultured eleven times. All of them were sensitive to Mino-

cycline. Seven of them were sensitive and four were resistant to other tetracyclines. All the staphylococcus aureus coagulase positive disappeared after treatment with Minocycline.

Five patients did not respond to treatment. One case, although improved clinically, had a positive culture four days after cessation of therapy. This patient had Bronchiectasis with acute Bronchitis. The organisms cultured were Proteus Mirabilis and Alpha Streptococcus Viridans. Four other patients did not improve clinically and their cultures persisted positive after cessation of therapy. They were the following:

1. Patient with acute Myeloblastic Leukemia and Pneumonia. Sputum showed Paracolon Klebsiella and Paracolon aerobacter sensitive to Minocycline.
2. Patient with Chronic Myelocitic Leukemia and Pneumonia in left upper lobe. Sputum culture showed Klebsiella, Proteus Mirabilis and Alpha Streptococcus Viridans. All of the organisms were sensitive to Minocycline.
3. Patient with the urinary tract infection whose culture showed E. Coli, Proteus vulgaris and Beta enterococcus. All of the organisms were resistant

to Minocycline.

4. Patient with urinary tract infection. Urine culture showed *E. Coli* and *Alpha enterococcus* resistant to Minocycline.

During the period of treatment, no secondary bacterial invaders were reported. No allergic manifestations were reported either. Only one patient with acute Otitis media had severe dizziness which disappeared when she discontinued therapy.

Serum glutamic exalacetic transaminase, serum glutamic pyruvic transaminase and serum lactic dehydrogenase were done in each case before starting treatment, on the fifth to seventh day of treatment and four to five days after cessation of treatment. Three of the patients had mild liver disease with slight elevation of these serum enzymes. Another patient had liver congestion secondary to congestive heart failure with slight elevation of the serum enzymes. No changes in the initial values of the serum enzymes was observed during the period of treatment in the patients with liver involvement. No change in the serum enzymes was observed in the rest of the patients treated with Minocycline.

Repeated hemoglobin, blood urea nitrogen and urinalysis failed to show any abnormal changes during the period of treatment in the fifty cases studied.

Renographic studies were performed in twelve patients before starting treatment, on the fifth to seventh day of treatment and four to five days after cessation of treatment. All the patients, except one, showed a completely normal pattern. These patterns remained normal during the period of treatment. One patient had a mild nephrotic syndrome with an abnormal renographic pattern. No worsening of this pattern was observed while the patient was on treatment,

that is, the same pattern persisted during the period of treatment and five days after cessation of therapy.

Summary

Fifty patients with different types of infections were treated with Minocycline, two hundred milligrams as initial loading dose followed by one hundred milligrams every twelve hours for ten days.

Forty five patients with infection caused by gram negative as well as gram positive organism including staphylococcus aureus coagulase positive showed good response to treatment. Five patients showed poor response with persistent infection after cessation of therapy.

Among the group that responded well to treatment, eighteen had a mixed flora and twenty seven had only one organism producing the infection. In eleven instances staphylococcus aureus coagulase positive was cultured, all of which were sensitive to Minocycline and responded well to treatment.

No changes were observed in transaminases and lactic dehydrogenase levels during the period of treatment. No abnormal urinary findings or change in renographic tracings were observed.

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Editorial

UTILIZATION, NUISANCE OR NECESSITY?

For the practicing physician, Utilization is something to stay; it involves both efficient rapid bed utilization and Medical Audit, the evaluation of quality of medical care. Peer review is mentioned nowadays, both in the corridors of organized medicine and the Halls of Congress; its definition is well expressed in the Manual on Peer Review, published by the American Medical Association:

"Peer review is evaluation by practicing physicians of the quality and efficiency of services ordered or performed by other practicing physicians. It is an all-inclusive term for medical review efforts. Medical practice analysis, in-patient hospital and extended care facility utilization review, medical audit, ambulatory care review, and claims review are all aspects of peer review."

This involves, obviously, time and lots of efforts of already busy clinicians who are hard-pressed by their Hospitals to perform Committee work as required by the Medicare Act and the Joint Committee on Accreditation of Hospitals. Without a properly functioning Utilization Review Committee, or a Record Room Committee quality of care quickly becomes jeopardized. Medical Audits should be performed on a Departamental basis since standards of care may vary to some degree by areas of practice and specialty and are best examined on the local level.

In order to evaluate and advise hospitals in the Metropolitan area on their Utilization Review Committee, the Central Committee on Utilization visited on a "Trial-type-Basis" the following hospitals:

1 Community Hospital (Presbyterian Community Hospital)

4 Private Hospitals (Hospital General San Carlos)

(Professional Hospital)

(Hospital del Maestro)

(Hospital Matilde Brenes)

1 Extended Care Facility (Hogar Carmelitano)

2 Government Hospitals (Centro de Salud de Bayamón)

(Hospital Distrito Universitario)

From these visits, our Committee got the following impressions:

I - That every Hospital has its faults, and that obviously no one has a perfect Utilization Review Committee. Most at fault seems to be the lack of clerical help where minutes of both weekly and monthly reviews are not prepared sufficiently. Help of the Record Room Librarian and a part-time Secretary is urgently needed. Furthermore, the Record should be well documented otherwise no Utilization Review Committee or claim reviewer can study it.

II - The problem of lack of Certification and Recertifications continues to haunt us; to call physicians back for a signature or description of clinical signs (not diagnosis) on a certification form seems red-tape to many of us, but not to those in charge of paying the Hospital Claim. Consequently, a part-time clerk or assignment of this important role to an existent administrative officer will save the Hospital great financial suffering later.

III - All patients should be included in a Utilization Review plan - not only those that have Medicare. This obviously, alleviates congestion for all patients for an already overworked Admission

officer. The rising costs of Health Care in Puerto Rico can be turned down by doing many procedures on an out-patient basis, by cutting down hospitalizations over the weekend or admission on Fridays and shortening hospitalization on all patients, whether with or without prepaid medical plans.

IV - The lack of in-hospital review prior to the so called "prolonged stay" period. Many patients could be discharged in our experience if after 2 to 3 days in the Hospital, an active Utilization Review Committee would indicate diplomatically, that further in-hospital care is not longer justified. The Utilization Review Committee plan provides for the mechanism in case of discord or difference of opinion.

V - Most of the private hospitals have medical and ancillary services that respond quickly to the needs of the in-hospital patient (e.g. Radiology, Laboratory and Consultation studies). This cannot be said, however, of the Governmental Facilities we visited. There, the lack of incentive, lack of efficiency no matter the dedication of many fine technicians are obvious and produce a picture of different design. Especially in view of the great multitudes of patients that are attended in the Government Facilities, it seems to us that these Medical and Ancillary Facilities are so important. Each report that is lost or delayed, each X-Ray film that is repeated makes less money available to the indigent medical care and makes hospitalization lengthier. It seems to me that urgent **Diversion and Decentralization** are needed here: Medicare, ACA, Prepaid Medical Plans can be diverted to the Private Sector, naturally, preserving the patients right towards free-choice; the idea of promoting possibly free-choice of-physician on an out-patient basis only (as a first step) seems to be an excellent one.

We all talk about in-patient care, but what about the Extended Care Facility? What does one do with the 82 year old patient with Arteriosclerotic Heart disease, diabetes mellitus and leg ulcer, who has been delivered by a well-meaning neighbor at the Emergency Room, has been admitted and is obviously improving but with no place to go, whose only son is a drug addict and no other family? What does one do in a society where children deliver a parent to a Hospital, refuse to visit the patient or to accept the parent home again? Should not one talk about responsibility rather than right? Are not there changes needed in political philosophy?

This leaves the Utilization Review Committee with an unsolvable problem that should be solved in a human way. Frequently, the Extended Care Facility does not accept this type of patient and the problem goes back in the lap of the Utilization Review Committee. We do need more facilities of this type and more perhaps people to staff these. I urge, therefore, more facilities of extended care or Nursing Homes and particularly visiting Nursing Services.

Last, but not least, let me say that no Utilization will work unless incentive and efficiency rewards are present. Even if this remuneration is minimal, it gives the members of the Committee a feeling of responsibility and the rewards for a well functioning Utilization Review Committee are multiple for a Hospital that has to present well documented minutes to an inquiring and sometimes doubtful Carrier. Needless to say, that accurate and adequate documentation of the medical record is the basis on which the Inspector draws his conclusions and it behooves us as physicians to put our clinical findings clearly in writing. Utilization then becomes an exercise in quality of medical care and an educational challenge which can stimulate an otherwise dull staff meeting.

Walter Kleis, MD

CARTA A LA REDACCION

Dr. Jorge O. Just Viera
Presidente, Junta Editora
Boletín de la Asociación Médica de Puerto Rico,
Santurce, Puerto Rico

Estimado Dr. Just:

Como asiduo lector del Boletín de la Asociación Médica de Puerto Rico durante muchos años, desearía hacer algunos comentarios, para publicación en el Boletín, sobre lo que a mi juicio es una tendencia lamentable de esta publicación nuestra.

El Boletín empezó como una revista médica en español. Al cabo de unos años se hizo bilingüe, y ahora, de algún tiempo a esta parte, el inglés parece ser su vehículo principal de expresión. Los anuncios y las noticias, que antes eran en español, ahora son en inglés; y, en el último número, noto que el editorial es en inglés.

¿Qué nos pasa a los médicos puertorriqueños? ¿Es que no podemos decir lo que sabemos en nuestro propio idioma, o es que tenemos tan poco aprecio por nuestra lengua vernácula, que nos negamos a honrarla y darle prestigio?

Lo que pasa en el Boletín es un reflejo de lo que pasa en nuestras asambleas médicas, donde apenas se oyen trabajos científicos en español, y en ciertos hospitales privados, donde hasta los avisos a los pacientes y visitantes son en el idioma inglés.

No tengo nada contra el lenguaje inglés. Hice todos mis estudios profesionales en los Estados Unidos, y me doy perfecta cuenta de la importancia de ese gran idioma en el campo científico; pero me apena ver el poco esfuerzo que hace el médico puertorriqueño por dignificar su idioma vernáculo. Tal parece que no sentimos orgullo en aprenderlo bien ni en conservarlo. Algunos médicos jóvenes (incluyendo graduados de nuestra escuela de medicina) desconocen la terminología de su profesión en español, y no hacen esfuerzo alguno por aprenderla. Prefieren ocultar esta deficiencia cultural haciendo sus presentaciones científicas en inglés, aun cuando sus oyentes sean sus propios paisanos. Esto es lamentable, y puede perjudicarnos en el natural deseo que todos tenemos de ganarnos el respeto de nuestros colegas de habla hispana, dentro y fuera del hemisferio.

Nuestra clase médica no parece darse cuenta cabal de la parte de responsabilidad que le corresponde en la conservación y dignificación de nuestra cultura hispánica. Está bien que publiquemos trabajos científicos en inglés en el Boletín de la Asociación Médica de Puerto Rico; pero esta publicación debe mantenerse como una revista médica predominantemente en nuestra lengua vernácula. Debemos tener orgullo en que así sea; si no por otra razón, por respeto propio.

Fraternalmente,

J. Rodríguez Pastor, MD

NOTICIAS

"PSYCHOPHARMACOLOGY AND THE AGING PATIENT," MAY 29-31, 1972

A conference to discuss the clinical use of psychoactive agents and the recognition and management of psychiatric syndrome of the elderly. Center for the Study of Aging and Human Development, Duke University, Durham, North Carolina. For further information write to Mrs. Dorothy Heyman, Box 3003, Duke University Medical Center, Durham, North Carolina 27710.

PROGRAMA CIENTIFICO AUSPICIADO POR LA SUB-REGION DE CAGUAS (Y COAUSPICIADO POR EL HOSPITAL SUB-REGIONAL Y LA ACADEMIA AMERICANA DE MEDICOS DE FAMILIA CAPITULO DE PUERTO RICO), QUE SE CELEBRARA DURANTE EL AÑO 1972:

1. Martes 22 de febrero de 1972 - Salón de Conferencias Hospital Sub-Regional - Use and abuse of Laboratory tests by doctor Germán Lasala (Chief Pathologist Sub-Regional Hospital).
2. Martes 25 de abril de 1972 - Conferencia Las Eczemas por doctor Raúl Morales, Jefe Depto. de Dermatología, Hospital Sub-Regional.
3. Martes 23 de mayo de 1972 - Ansiedad y Depresión - doctor José A. Núñez, Jefe Centro de Salud Mental.
4. Martes 27 de junio de 1972 - Surgical Correction of Cleft palate and Lip: by doctor Armando Barreto, Plastic Surgeon.
5. Martes 22 de agosto de 1972 - Management of Trauma on an Emergency Basis: by doctor Sergio Delgado Muñoz, Chief Orthopedist Surgeon Sub-Regional Hospital.
6. Martes 25 de septiembre de 1972 - Rol del Médico de Familia en el manejo del paciente Adicto a Drogas: by doctor José A. Núñez López, Director Centro Salud Mental.
7. Martes 28 de noviembre de 1972 - Papanicolau Usos, interpretación, Técnica: by doctor José Vargas Cordero, Chief OB-GYN y doctor Eliud López Patólogo.

NOTA: Todas las conferencias comenzarán 8:00 p.m. y se celebrarán en el Salón de Conferencias - Sub-Regional Caguas, Puerto Rico.

HEXACHLOROPHENE MERRY-GO-ROUND:

The U. S. Food and Drug Administration is developing reservations concerning the safety of hexachlorophene following reports that untoward results have been observed in rats and monkeys previously exposed to the drug in abnormally large quantities.

Such reports should be interpreted with great caution. In the case of the experimental rats the animals were fed hexachlorophene. No one has ever recommended the oral route for human beings. In the case of the baby monkeys, one authority estimates that from four to six times greater amounts were used than is customary for humans.

The FDA, in announcing restrictions on the use of hexachlorophene, stated that there has been no evidence of harm to humans when it is used as recommended. One of the standard cautions has been for careful clear water rinsing after bathing.

One encouraging development is the calm and unexcitable reaction of the Canadian Health Department's food and drug directorate. The head of the directorate said that the bacteria-destroying chemical has been used without ill effect for more than 20 years to bathe newborn infants. Other than advising physicians to ensure careful compliance with instructions for proper use the Canadian said further that his committee would monitor further developments and would not change policy until results of experiments were known.

The backlash effect in the United States is already evident. There are reports of nurseries wherein epidemics of staphylococcal skin disease have developed following discontinuance of hexachlorophene bathing.

It doesn't take a very long memory to go back to pre-hexachlorophene days when such epidemics were stubborn and dangerous - sometimes being associated with fatalities.

Further animal experimental studies are being done. In view of the fact that no human toxicity under normal use conditions has ever been reported it would seem to be wise to await the additional information which will be provided.

(Being published in March 1972 issue - Journal of the Indiana State Medical Association - Permission to copy granted by Frank B. Ramsey, MD)

BNDD REVIEWING ABUSE POTENTIAL OF BARBITURATES:

Bureau of Narcotics and Dangerous Drugs is reviewing medical and scientific data on barbiturates and preparing a survey on their use and abuse. A BNDD source said that contrary to some press reports, the agency has not taken a definitive position on whether to place barbiturates under stricter controls, as some drug abuse groups have urged. Barbiturates are now listed in schedule III of the controlled dangerous substances. Although the bureau recognizes that barbiturate abuse exists, the source said, it wants to gather more information to determine whether the abuse warrants further control. It had been reported that BNDD Director John Ingersoll would

announce plans to bring the drug under tighter regulation at a hearing of the Senate juvenile delinquency subcommittee (Judiciary). The sessions, scheduled for March 9 and 10 by Chairman Birch Bayh (D., Ind.), have been indefinitely postponed. Last month Food and Drug Commissioner Charles Edwards testified at a House health subcommittee hearing that the agency is considering barbiturates for stricter control and a recommendation is expected within a few months. Some medical experts have argued that more restrictive classification of the drug would be impractical and unwise due to the drugs' varied medical uses, because abuse is usually characterized by patients taking excessive amounts of prescribed medicine, and because there are many different products on the market with a wide range of dosage forms.

REPRESENTATIVE MILLS DISCUSSES HEALTH CARE:

Rep. Wilbur D. Mills (D) Ark., Chairman of the House Ways and Means Committee, outlined his feelings on national health insurance and related health care subjects in an address to the Second National House Staff Conference Institute for the Study of Health and Society. Mr. Mills said that the government could assist in the health care insurance area "by providing the mechanism under which virtually every American family, regardless of its situation, will have the same basic coverage at about the same price. And," he said, "I believe that we can do it without having to place on the Federal bureaucracy the entirely impossible administrative task of managing our entire health complex." He set forth three major elements of his plan for providing uniform insurance benefits for all members of society: (1) mandated health coverage for the employed, with cost sharing between employers and employees; (2) a new program of health care for the poor, providing uniform benefits "at least as comprehensive as those available to middle income groups;" and (3) nationwide options, under government auspices, to provide health insurance to the self-employed and certain small employers. As a supplement to the basic health insurance plans, Mr. Mills recommended the adoption of a catastrophic health insurance program related to a family's taxable income. In addition to his proposals for health insurance, Mr. Mills again called for expansion of Title V Maternal and Child Health programs.

OTROS PUNTOS DE VISTA

"SOMEONE SHOULD TELL THE FDA"

As a result of a clinical investigation which found that several preparations of digoxin varied markedly in bioavailability even though they were all equal by USP chemical standards, the Food and Drug Administration will run tests on digoxin products for biologic equivalence.

Last year clinicians of Columbia University College of Physicians analyzed four lots of digoxin because of observations that patients were responding atypically to carefully planned therapeutic schedules. The four lots of tablets were found to be chemically equal and within USP requirements. However, when administered to normal volunteers the serum levels were found to vary markedly. In one instance the serum level was seven times that obtained for one of the other products.

Several of the patients were noted to have low serum

levels of the drug even though they received as much as 1.0 mg daily. The clinicians recommended that evidence of biologic equivalency of digoxin products should be required in addition to chemical equivalence.

This clinical report has prompted a natural and reasonable response by the FDA — tests will be run on some digoxin products for biologic equivalence.

However, other responses from the FDA have not been so rational. One response is that, while there is need to inquire into bioavailability, the across-the-board requirement of biologic equivalence in drugs is too knotty for immediate official action.

Another response is the FDA announcement that chemical analyses have shown some batches of digoxin which showed variations of from 60 percent to 200 percent of the declared amount of the active ingredient.

Another FDA response is the statement that biologic equivalence is considered by some to be a minor problem, by others a major consideration, and that FDA just does not presume to have the final answers.

There is also the quotation that one FDA official asks "At what point do you stop applying the principle of requiring bioequivalence in drugs?" This seems a rather useless worry when it is considered that FDA hasn't even started applying the principle as yet. Someone should tell FDA that digitalis preparations would be a good place to start.

For a drug for which the proper therapeutic serum level is narrow and is balanced between a practically ineffective level when too low or a toxic effect when too high, and where individual patient tolerances, and the effects of concomitant medication introduce significant variables, it is folly to work with a formulation entirely bereft of either chemical or biologic equivalence, and even worse without both.

The FDA has been so busy eliminating time-tested and clinically valuable pharmaceuticals from the market that it has neglected to require that potent drugs like digitalis be manufactured in reliable form.

(Being published in the February 1972 issue- Journal of the Indiana State Medical Association - Permission to copy granted).

TRAGIC MISADVENTURE WITH HEXACHLOROPHENE

The Food and Drug Administration has been trying to wake up from what the Associated Press calls a "regulatory nightmare" on its hasty, precipitate ban on hexachlorophene bathing of the newborn. Specifically indicted in the FDA ruling was pHisoHex (Winthrop), a product about as well established in the health care field as shoes are in our clothing customs.

Save for the tragic consequences growing directly out of the restriction, the whole matter could be characterized as just another regulatory misadventure which, against the record of oral contraceptive scares, combination ingredients bans, and once, the labeling of a tennis shoe as a drug, should astonish absolutely nobody at all.

The entire point is simply this: When the preliminary and obviously inconclusive findings suggesting some degree of hazard in hexachlorophene bathing surfaced, the medical profession — or more specifically, the American Academy of Pediatrics — acted promptly, decisively, and effectively to recommend measures to protect the newborn. And what's

more, physicians know that they can best rely on the advice of other physicians who weigh the risk-versus-benefit ratio as only physicians can.

The HCP ban was based upon three preliminary reports:

— Fifty newborn infants bathed with a 3 percent HCP product in the hospital nursery were said to show blood levels of the agent of .009 to .646 mg/ml at discharge. But, incredibly, the same report stated that "no obvious toxic symptoms were noted in the newborns."

— Rats fed (yes, it said *fed*) hexachlorophene to achieve mean levels of 1.21 mg/ml showed brain changes.

— Newborn monkeys washed daily with a 3 percent HCP product for 90 days showed mean plasma levels of 2.3 mg/ml and brain changes at autopsy. But now, it develops, the scientists conducting the investigation concede that the baby monkeys were not tethered during their baths, so just how much bathwater was ingested under such circumstances cannot be known.

The Journal reported in February that staph outbreaks were occurring in hospital nurseries where use of HCP had been discontinued. A few days after the Journal appeared, FDA held a news conference, making the tragic succession of events public. The agency crawled a little, too, saying that physicians didn't really understand what it had said in its Dec. 6, 1971, bulletin. The other inference was that it didn't mean what it said.

There is a lesson here, albeit at the tragic expense of regulatory conclusion—jumping and the health of newborn infants. Physicians acted promptly to advise their colleagues of the tentative findings. And other physicians listened. So the FDA's action was at worst a monumental goof and at best, a poorly managed action of the bureaucracy.

We are not talking about "what" but "how". And we maintain that these matters are best left in the competent, experienced

hands of the medical profession whose sole concern is the preservation and improvement of the quality of life. — R. B. K.

(March Issue)

We quote letter received by the American Medical Association from Alfred A. Russell, Chief Registration & Audit Division, United States Department of Justice, Bureau of Narcotics and Dangerous Drugs, Washington, D. C.:

"I would like to request your assistance at this time in publicizing the fact that effective May 1, 1972, only Bureau of Narcotics and Dangerous Drugs Official Order Forms will be valid for transactions involving Schedule I and II controlled substances. Any practitioner may obtain the new forms by forwarding the old type IRS order form requisition (IRS Form 679) to the BNDD Registration Branch, P. O. Box 28083, Central Station, Washington, D. C., 20005.

The registrant's complete, nine-character BNDD registration number must be shown on the form in order that it may be processed. IRS Form 679 will not be honored as a valid requisition for official order forms after April 30, 1972. Therefore, this type requisition should be submitted as soon as possible. Any registrant who does not have an IRS requisition, and who desires the new order forms, is required to complete form BND 222D and forward it to the Registration Branch. The BND 222D forms may be obtained from the Registration Branch or any BNDD Regional Office.

It would be a tremendous help to this Bureau's order form operation if the above information could be channeled to the various state and local Medical Society publications.

Thank you for your cooperation in this important matter."

— A N U N C I O S —

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Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

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El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

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Nomenclatura: Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas: Las tablas deben aparecer en hojas separadas. Estas deben incluir el título y el número de la tabla (romano). Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla.

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SESION CIENTIFICA ANUAL

Septiembre 30 y octubre 1ro. de 1972

Hotel Caribe Hilton

San Juan, Puerto Rico

ABSTRACTOS

El Comité Científico invita a enviar abstractos de trabajo originales para considerarse para la Convención Anual que se llevará a cabo el 30 de septiembre y el 1ro. de octubre de 1972 en San Juan.

Procedimiento:

- 1. Enviar un abstracto de 250 palabras o menos en maquina a doble espacio. Se necesitarán un original y tres copias.*
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 - f) Equipo audiovisual que se requiere para la presentación.*
- 3. Enviar lo anterior a: Amalia Martínez Picó, M. D., Presidente del Comité Organizador, Asociación Puertorriqueña del Corazón, Apartado 8215, Fernández Juncos, Santurce, Puerto Rico, 00910.*

LA FECHA FINAL PARA RECIBIR LOS ABSTRACTOS ES JULIO 15 DE 1972.

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Precautions: In the elderly and debili-

tated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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BOLETIN

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Isco X. Veray, MD, Ryan P. Crenshaw, MD, Waldo López, MD, FACP, Jorge Gandía, MD, Raúl Yordán, MD and Iván Pelegrina, MD, FACOG

ACUTE TRIFASCICULAR BLOCK — A REPORT OF FOUR CASES AND A
REVIEW OF THE LITERATURE 103

Pablo Iván Altieri, MD and Charles Johnson, MD, FACP

HYPERLIPOPROTEINEMIC TYPES AMONG PUERTO RICANS: A PROGRESS REPORT 111

Marta Cancio, PhD and José M. León, BS, MT

PREVENTION OF COMPLICATING EMOTIONAL PROBLEMS OF THE PARAPLEGIC 119

Herman J. Flax, MD, FACP

EDITORIAL 122

NOTICIAS 124

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The negative power of undue anxiety
in congestive heart failure...

This man thinks he can no longer
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Typical of many patients with congestive heart failure, he also suffers from severe anxiety, a psychic factor that may influence the character and degree of his symptoms, such as dyspnea. His apprehension may also deprive him of the emotional calm so important in maintenance therapy.

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Specific medical and environmental measures are often enhanced by the antianxiety action of adjunctive Libritabs (chlordiazepoxide). Libritabs can also facilitate treatment of the tense convalescent patient until antianxiety therapy is no longer required. Whereas in geriatrics the *usual daily dosage* is 5 mg two to four times daily, the *initial dosage* in elderly and debilitated patients should be limited to 10 mg or less per day, adjusting as needed and tolerated.

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six.

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up to 100 mg daily
for severe anxiety
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tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close observation. Obtain a detailed history, and complete blood and laboratory examination (complete blood count, urinalysis, etc.) before prescribing and at regular intervals thereafter. Carefully select patients, especially those responsive to routine measures, and do not treat patients or those who cannot be observed closely. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the lowest possible dosage is the goal of therapy. The drug should be taken with meals or a full glass of water. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral ulcers, symptoms of blood dyscrasia; dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools; other evidence of intestinal ulceration or bleeding; skin reactions, significant weight gain or loss. A one-week trial period is adequate. Discontinue the drug in the absence of a favorable response. Restrict dosage to one week in patients over sixty. **Indications:** Acute gouty arthritis, rheumatoid arthritis, ankylosing spondylitis.

Contraindications: Children 14 years or less; senile dementia; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent ulcers; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypothyroidism; thyroid disease; systemic edema; enlargement of salivary gland enlargement due to the disease; myalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic drugs; long-term anticoagulant therapy. **Precautions:** Age, weight, dosage, duration of therapy, presence of concomitant diseases, and concurrent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who may have increased susceptibility to the toxicity of the drug. Use the lowest effective dosage. Weigh initially to obtain maximum benefits against potential risk of severe, adverse reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

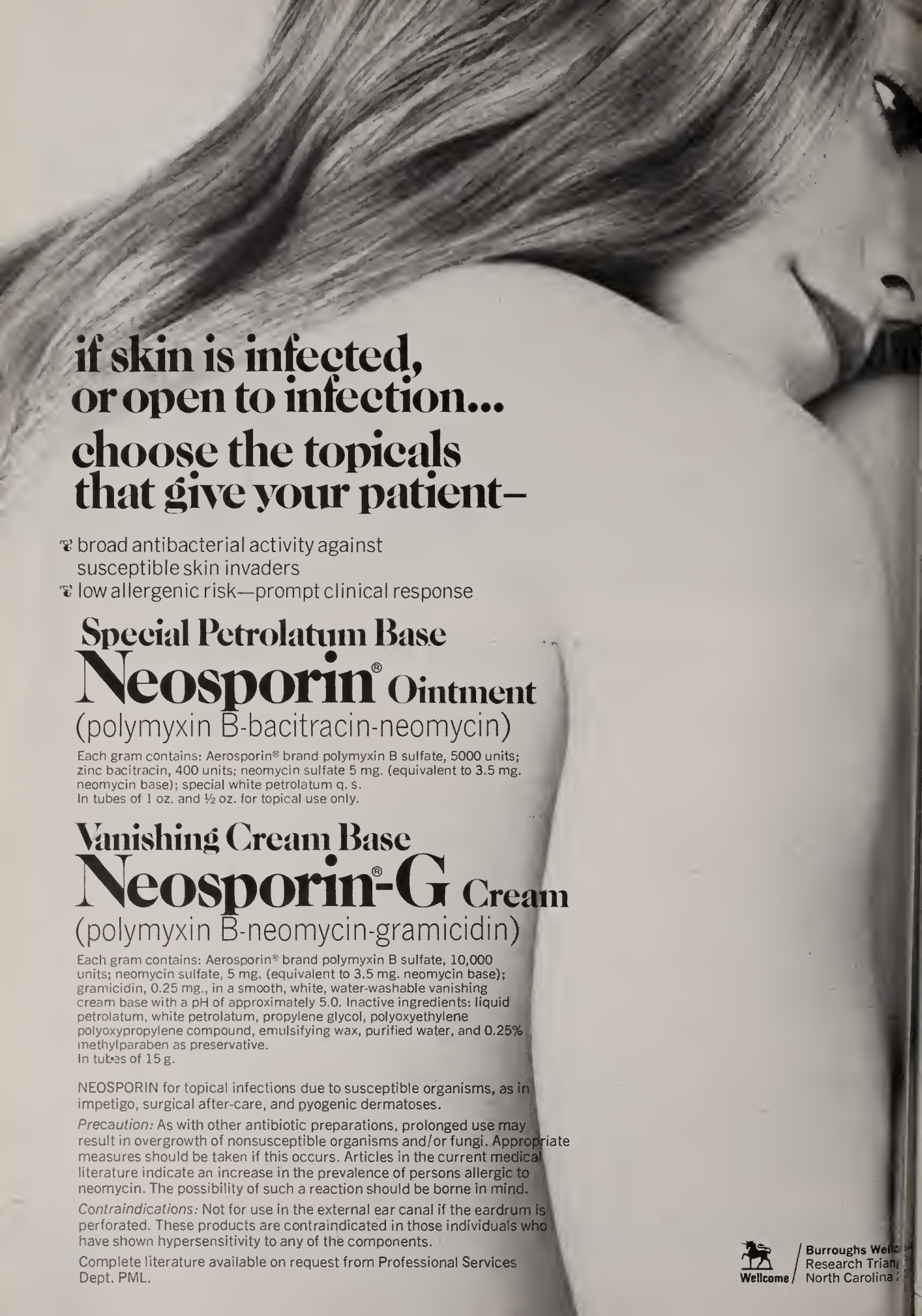
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B) 98-146-800-E

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that give your patient—**

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In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
Neosporin[®]-G Cream
(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin[®] brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

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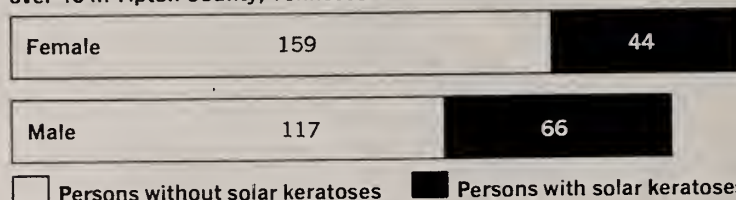
What it means to live and work in Tipton County, Tennessee

**Persons who are white and
over 40 have one chance in four
of having solar keratoses...
which may be premalignant**

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

**Prevalence of solar keratoses in white persons
over 40 in Tipton County, Tennessee**



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Solar, actinic, senile keratoses

Called by many names, the typical lesion is flat or slightly elevated, brownish or reddish in color, papular, dry, adherent, rough, sharply demarcated; usually multiple lesions, chiefly on exposed portions of the skin.

Sequence/selectivity of response

Erythema in areas of lesions may begin after several days of therapy; height of reaction (erythema in affected areas)* usually occurs within two weeks, declining after discontinuation of therapy. Since this response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

Cosmetic results

Cosmetic results are highly favorable. Incidence of scarring is low—important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

5% cream—a Roche exclusive

Roche formulates the 5% cream... high in patient acceptability... high in clinical efficacy, especially for lesions of hands and arms... economical.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

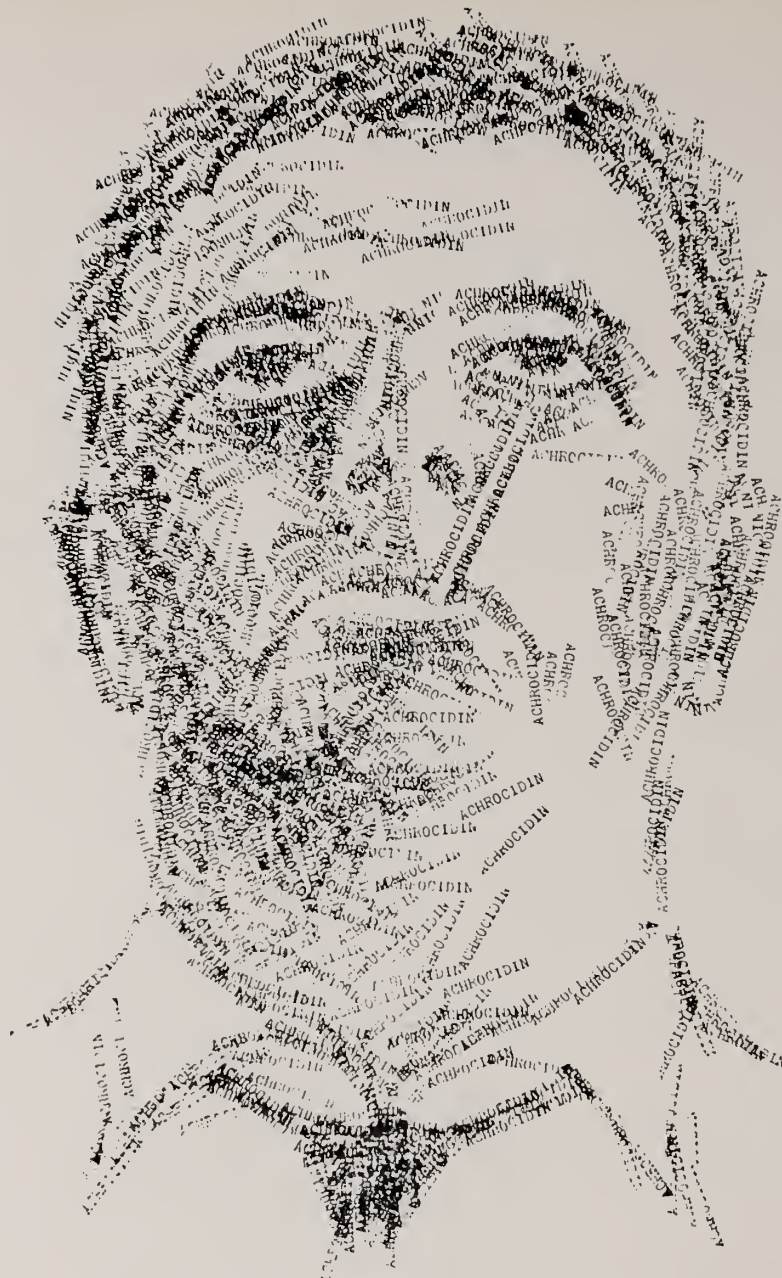
Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

an alternative to conventional therapy **Efudex[®]** (fluorouracil) cream/solution



Roche Laboratories
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Achrocidin[®] Tablets and Syrup

Tetracycline HCl—Antihistamine—Analgesic Compound

Each tablet contains: ACHROMYCIN[®] Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Caffeine 30 mg.; Salicylamide 150 mg.; Chlorothen Citrate 25 mg.

ACHROCIDIN Tetracycline HCl—Antihistamine—Analgesic Compound Tablets and Syrup are recommended for the treatment of tetracycline-sensitive bacterial infection which may complicate vasomotor rhinitis, sinusitis and other allergic diseases of the upper respiratory tract, and for the concomitant symptomatic relief of headache and nasal congestion. For children and elderly patients you may prefer caffeine-free ACHROCIDIN Syrup. Each 5 cc contains: ACHROMYCIN Tetracycline equivalent Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Salicylamide 150 mg.; Ascorbic Acid (C) 25 mg.; Pyrilamine Maleate 15 mg.

Contraindications: Hypersensitivity to any component.

Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.

Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons

on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculo-

popular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, discoloration. *Kidney*—dose-related rise BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis high dosage.

Upon adverse reaction, stop medication treat appropriately.



LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York 10965

TAKAYASU'S ARTERITIS IN PREGNANCY

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Takayasu's arteritis (Pulseless Disease) is an entity occurring in young females, characterized by a chronic, progressive inflammatory process of the aortic arch, as well as of the carotids, the subclavian, the axillary and other arteries. It forms part of the aortic arch syndrome (Martorell and Fabre (28, 29, 30), 1944, Frovig (16), 1946, Ross and McKusick, 1953 (31), a concept elaborated by several authors years ago.

Although this process is most frequent in young females—starting at the second and third decade—(2, 3) very rarely has it been related to pregnancy. Details are meager as to possible aids for diagnosis, management and future outcome of this disease in the child-bearing female. The only case found in the obstetrical literature reported as Takayasu's (41) arteritis lacks the usual laboratory findings. Angiocardiographic studies done were compatible with obstruction of the vessels arising from the aortic arch, and with absence of the left pulmonary artery. Thus, we believe that this case represents an odd variation of aortic arch syndrome and not a genuine case of Takayasu's arteritis.

In the following case reports it seems worthwhile to discuss the instances in which arteritis has been related to pregnancy, as well as the possible means of diagnosing it during pregnancy in the prenatal stage and during labor and the post partum period.

Case Reports

Case 1

This is a 32-year old colored female, Grave IX, Para VI, Abortions II, who was referred in her 32nd week of pregnancy to the Maternal and Infant Care Project Clinic of the University Hospital, because of albuminuria. Last menstrual period was on

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Part of this paper was presented at the Annual Meeting of the Puerto Rico Heart Association, September 1971, San Juan, P. R.

July 2, 1966 and the expected date of confinement was set for April 6, 1967. On the first appointment to the clinic the nurse found that the patient did not have pulse or blood pressure in her upper extremities.

The patient gave past history as follows: She had a fever of unknown origin at age 21, which subsided spontaneously after being intensively worked up and treated by her family physician. It was then that the patient was told that she did not have pulses in her upper extremities. Five years ago she developed recurrent fever and polyarthralgias. She was referred to the University Hospital from the Local Health Center where she had been treated with "some white pills". At the University Hospital the patient was told to have a heart murmur. Since then she has complained of occasional palpitations and throbbing headaches localized in the temporal region, alternating with ear aches radiating to her jaws. She also gives history of dizziness and episodes of syncope lasting few seconds (specially upon assuming an erect position) sometimes accompanied by sensation of dullness in both upper extremities. This sensation is worsened after cradling her children for a while. At other times she complained of tired-

ness and coldness of her hands. Lately she has had moderate shortness of breath upon exertion and burning sensation in chest, upon strenuous exertion, lasting about half an hour. Eight years ago the patient had some genito-urinary trouble with decreased urinary volume and burning sensation. For this she was successfully treated at a Local Health Center.

Menarche at 16 years of age. Her menses were irregular, lasting 8-9 days. She was married at age 16. Her first pregnancy was at age 18 and this ended in spontaneous abortion of two months gestation. The patient has six children living and well. On March, 1966 she had another spontaneous abortion.

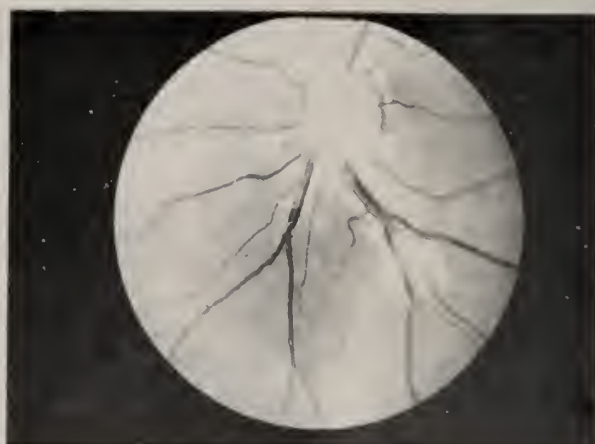
Family History: Non contributory.

Physical Examination: The blood pressure could not be obtained in upper extremities, but in the lower extremities it was 240/100 mm Hg. bilaterally. Apical pulse was 80 beats per minute and the respirations were 20 per minute.

The patient seemed older than her stated age, with mild muscle wasting of face and unexpressive "poker like" face. Normal ear drums and external canals. Normal eyelids, conjunctiva and sclerae. Funduscopic examination showed no obliterations, exudates, hemorrhages, aneurysms, or newly formed vessels (Fig. 1). Nasal septum was normal. Left carotid pulse was felt 3+ with a thrill felt in that area. The right carotid pulse is diminished (1+). Lungs are clear to auscultation and percussion. The point of maximum impulse was felt on the fifth left intercostal space at the midclavicular line. There is a grade 3/6 systolic murmur best heard in the right infraclavicular area, radiating to the neck. No evidence of cardiomegaly by physical examination. The rest of the physical examination was within normal limits. Uterus was

OD

OS



AV

Fig. 1: A. V. T. 1966: Fundusoscopic Examination of Right Eye (OD) and Left Eye (OS) showed no obliterations, exudates, hemorrhages, aneurysms or newly formed vessels. Ophthalmodynamometry showed; OD 45/90, OS 40/95.

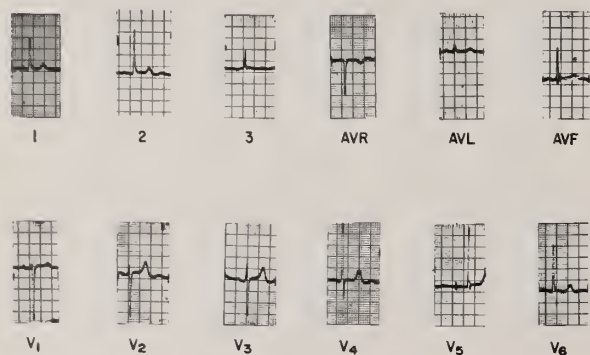


Fig. 2: A. V. T. 1966 Electrocardiogram showed left ventricular hypertrophy by voltage.

1 fingerbreadth above the umbilicus. Laboratory: Findings include a 24 hours urine protein of 0.23 gm. Sedimentation rate 54mm/hour, corrected to 40mm/hour. Series of LE cell preparation were negative. Hematocrit 35.5 percent, WBC 11,000, Differential count: Basophils 1, eosinophils 9, segmented 66, lymphocytes 24; total protein 7.2 grams percent, albumin 4.0 grams percent, globulin 3.2 grams percent, A/G ratio 1.2, VDRL negative, GTT (51 gm.) (True glucose) Fasting blood sugar 64 mg. percent, 1 hour - 65 mg. percent, 2 hours - 78 mg. percent, 3 hours - 80 mg. percent. Antinuclear antibodies negative. Electrocardiogram showed left ventricular hypertrophy by voltage (Fig. 2). Vectocardiogram (Fig. 3) was read as left ventricular hypertrophy.

The electrophoresis of proteins (Fig. 4) showed slight decrease in albumin with increased Alpha 2, Beta and Gamma Globulin (the gamma globulin increase is of the diffuse polyclonal type).

Subsequent admissions can be summarized thus: On February 22, 1967 the patient was admitted for evaluation

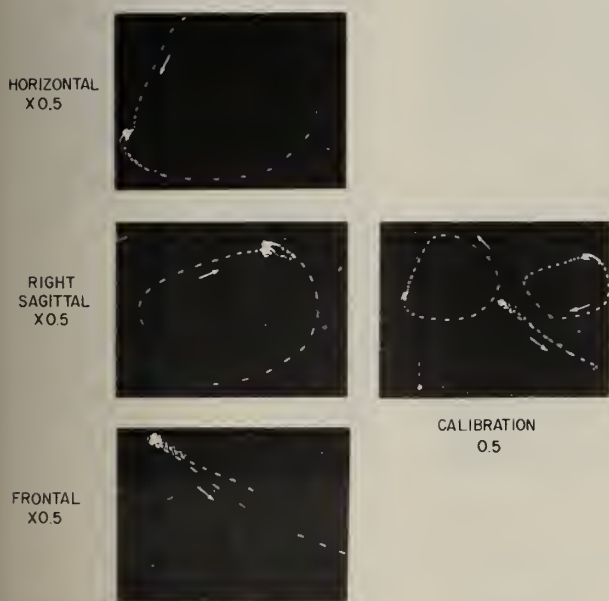


Fig. 3: A. V. T. 1966. Vectocardiogram showing left ventricular hypertrophy. (Using the Frank system)

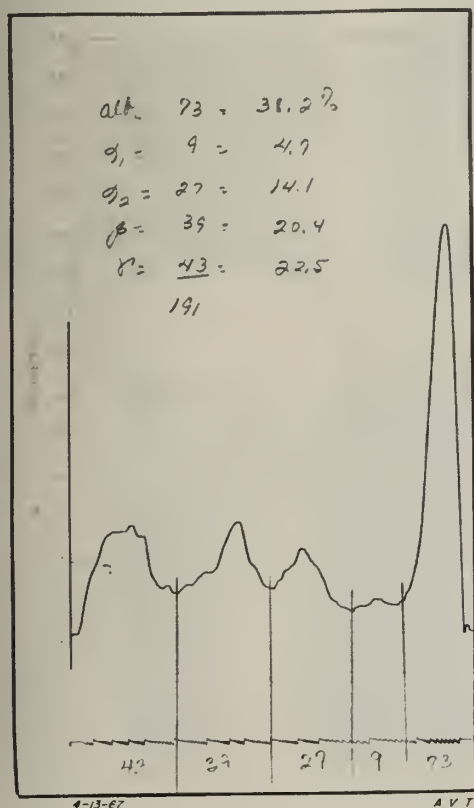


Fig. 4: A. V. T. Electrophoresis of proteins showing slight decrease in albumin with increased Alpha 2 and Beta. The gamma globulin are increased (diffuse type).

of her albuminuria and physical condition. She was placed on low salt diet, phenobarbital and bed rest. During her hospitalization the patient complained of headaches that cleared after low sodium diet and Phenobarbital, 30 mg. t.i.d., were started. The pain gradually subsided. On March 3, 1967, the patient was seen on consultation by the ophthalmologist, who found no gross abnormalities in the fundi. Ophthalmodynamometry showed: OD 45/90, OS 40/95. Consultation with physical medicine showed an essentially normal EMG with no electrical evidence of muscle myopathy. The chest X-ray examination, with shielding for protection of fetus, showed cardiomegaly with a cardiothoracic ratio of 13/24 centimeters associated with left ventricular preponderance and elongated aorta and mild vascular congestive changes (Fig. 5). Blood pressure in lower extremities 200/75 mm of Hg. Daily examination for albumin in urine failed to show any albuminuria after the third day in hospital.

She was discharged to be followed up in our clinic. On April 30, 1967 the patient gave history of vaginal bleeding and was admitted again to the University Hospital. Abdominal examination revealed the uterine fundus 3 fingerbreadths above the umbilicus. Fetal heart sounds 140/min. Speculum examination showed normal internal genitalia except for abundant, white, thick vaginal secretion. She had a positive Chadwick sign. The cervix was parous, enlarged and hypertrophic. No erosion was found.

The Papanicolaou smear was Class 1. On April 10, 1967 amniography was performed showing low lying placenta. The patient stayed in Hospital and was treated conservatively. She was discharged to be followed in the Maternal and Infant Care Project clinic. On May 25, 1967 the patient was admitted in labor. Measures were taken as to have blood cross matched in case a blood transfusion was needed. At 11:12 p.m., on May 26, 1967 she delivered, vaginally, a living male, in vertex presentation, LOA position, weighing 6 lbs. 1 oz., with Apgar score of 8 and 9 at 1 and 5 minutes. At 11:20 p.m. the placenta and membranes were delivered spontaneously. Post partum course was uneventful and she was discharged to be followed at the Obs.-Cardiac clinic. On August, 8, 1967 a right side femoral percutaneous catheterization was performed. The catheter was placed in the ascending aorta with 45 cc of 75 percent hypaque and an aortogram was performed. This showed an irregular external contour thoracic aorta, with increased thickness of its wall. Early films showed fair visualization of the innominate artery, right subclavian and right common carotid arteries, as well as of the left common carotid artery. No visualization of the left subclavian artery was noted (Fig. 6). The patient developed pruritus and a rash after the procedure that was controlled with antihistaminics. The patient was presented before the Sterilization Board for the progressive nature of her condition and multiparity and sterilization was approved in her case. On December 5, 1967 she underwent bilateral salpingectomy, tolerating the procedure well.

Case 2

This 22-year old female was first seen in our Prenatal Clinic on May 20, 1966, referred from a Health Center, because no pulse or blood pressure were found in her first prenatal visit. At the time she denied any history of polyarthrititis, fever, cough or general malaise. On June 16, 1966 the patient was admitted to the University Hospital for evaluation. She gave history of a right supraclavicular mass that was present



Fig. 5: A. V. T. X Ray No. 05-76-86. X Ray chest PA and lateral on 2/29/68. Showed cardiomegaly with a cardiothoracic ratio (C. T. R.) of 13/24 centimeters associated with left ventricular preponderance and elongated aorta. Mild vascular congestive changes.

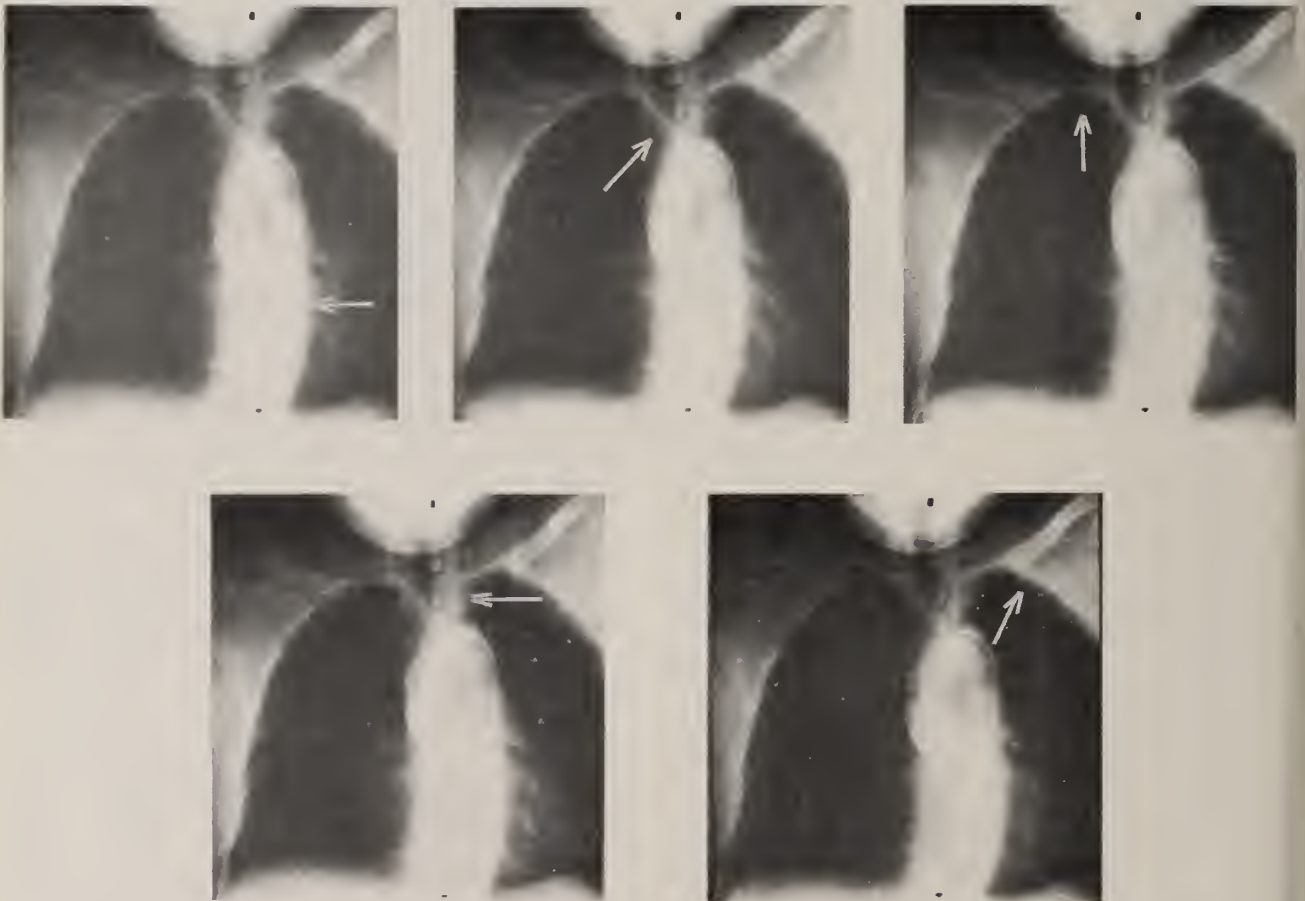


Fig. 6: Representative sequential films of a thoracic aortogram showing the thoracic aorta to have an irregular external contour with increased thickness of its wall (see arrows). Early films show fair visualization of the innominate artery, right subclavian and right common carotid arteries, as well as of the left common carotid artery. No visualization of the left subclavian artery was noted. Delayed films show retrograde filling of the left vertebral artery and faint visualization of the left subclavian artery, which is diminished in caliber (subclavian steal syndrome) (see arrows).

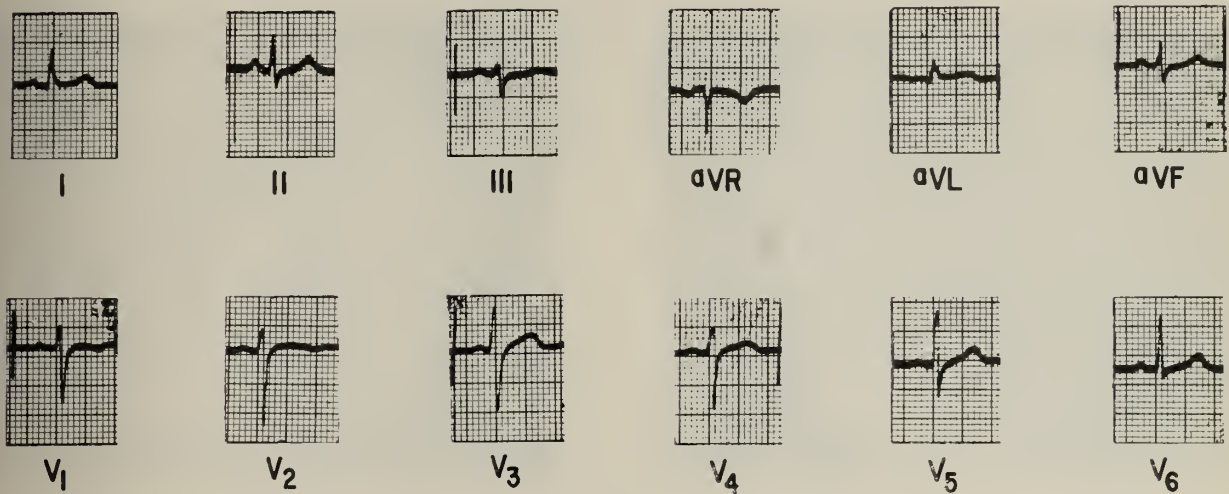


Fig. 7: J. R. M. June 13, 1966. 12 leads electrocardiogram within normal limits.

for one year. This mass was of variable size, non suppurative and non tender, and coincided with pain and weakness of her arms while ironing. She also complained of blurring of vision while standing up. She denied contact with tuberculosis. On physical examination the blood pressure was unobtainable in both upper extremities. The pulse was not felt in the left carotid, both antecubital, brachial and radial arteries and was felt weakly in the right carotid artery, diminished bilaterally in the dorsalis pedis arteries, and 2+ in the femoral arteries. There was no cardiomegaly but a soft Grade I-II systolic ejection murmur was heard over the aortic focus. A mass, the size of a "marble" was present in the right supraclavicular area. The fundus was essentially normal. Series of LE preparations were negative. Total proteins were 6.6, albumin was 3.75, globulin was 2.85; A/G ratio 1.3, Calcium was 11.3 mg. percent, alkaline phosphatase was 15.3 units, 2 hours post prandial blood sugar was 80 mg. percent (plasma). VDRL was non reactive. CBC was within normal limits so was the urinalysis. Several sputum examinations for acid fast bacilli were negative. Electrocardiogram was within normal limits (Fig. 7). Last menstrual period was on March 21, 1966 and her estimated date of confinement was December 28, 1966. Hospital course was uneventful. She was seen by the surgical consultant, who advised a biopsy of the right supraclavicular mass, but the patient left without medical advice and was lost for follow up. On December 3, 1966 she was admitted to another Hospital in the community, in labor pains. She delivered spontaneously a normal female baby. The mass in the supraclavicular area had disappeared. The patient was again lost for follow-up.

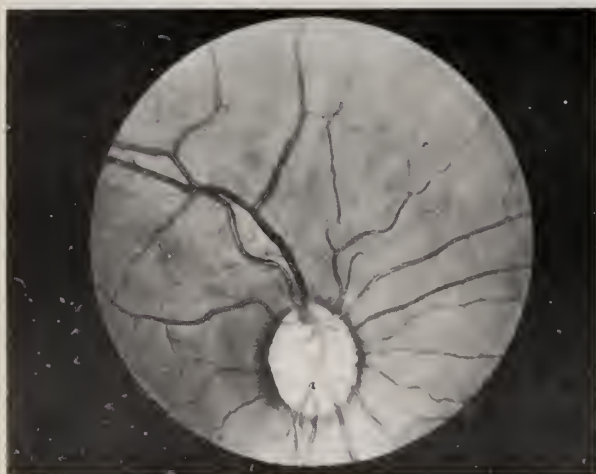
On December 18, 1968 she was admitted in premature labor to the University Hospital. Her last menstrual period occurred in March 21, 1968 and the expected date of confinement was December 28, 1968. She was found to have no pulse or blood pressure in the upper extremities. Blood pressure in lower extremities was 130/80. Left carotid pulse was not felt and right carotid pulse was +1. The chest was clear to auscultation and percussion. There was a grade one - two systo-

lic ejective murmur best heard in the aortic focus, radiating to the neck. The pulse showed occasional premature beats. She had a "poker face" expression and the upper muscles of her trunk seemed wasted. She claims to have frequent frontal headaches, throbbing in nature and accompanied by loss of visual acuity, specially after performing a hard work or a long walk. Eyegrounds were within normal limits (Fig. 8). Her arms get tired every time she does the laundry or irons her clothes. Electrocardiograms showed non specific ST-T wave abnormalities and frequent premature atrial beats with aberrant conduction (Fig. 9). Hematocrit was 45 percent. Total proteins were 7.17 gm. percent, albumin was 4.05 gm. percent, globulin was 3.12 gm. percent. Series of LE preparations were negative and so were the antinuclear antibodies. Urinalysis was within normal limits. Sedimentation rate was 11 mm/hour, serum electrophoresis was as follows: Albumin 46.7 percent, alpha 1, 3.7 percent, alpha 2, 9.3 percent, Beta 14.7 percent and gamma 25.7 percent (normal values in our Institution: Albumin 62.8 percent, Alpha 1, 1.9 percent, Alpha 2, 5.9 percent, Beta 6.1 percent, gamma 8.5 - 18.5 percent (Fig. 10).

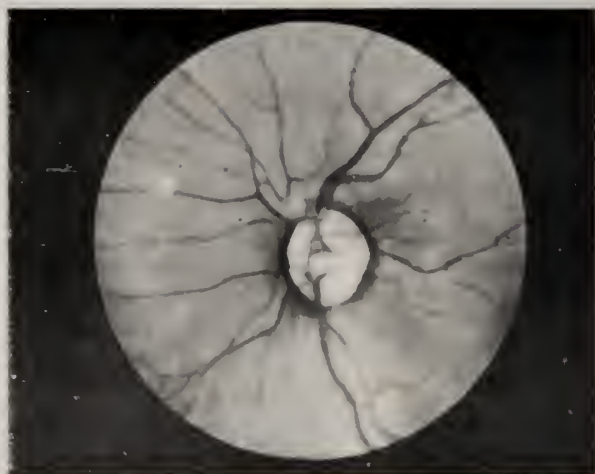
The patient delivered vaginally on November 16, 1968. Her post partum stage was uneventful and she was discharged to the follow-up at the cardiac clinic of our Institution.

P. P. D. done on December 17, 1968 was read as Gr. I positive (40 mm. 22 mm.). The same grading was made to the battey skin test (12 mm. 10 mm.). A series of lupus erythematosus preparations have been reported as negative. Chest X-ray showed cardiomegaly and a cardiothoracic ratio (C.T.R.) of 12.8/24.2 centimeters, associated with elongation of the aorta. The pulmonary vascularity was normally outlined and the lungs were clear (Fig. 11). The intravenous pyelogram was reported as normal with a calcification at the descending aorta. On March 11, 1969, using the right antecubital vein with an INH catheter placed in the pulmonary artery, an angiogram to observe the levo phase was performed. This procedure had to be used due to the difficulties in finding a femoral tributary for a retrograde angiogram, as even the femoral pulses were also diminished. The angiogram showed normal visualization

OD



OS



J. R.

Fig. 8: Funduscopy Examination of right eye (OD) and Left eye (OS) showed no obliterations, no exudates, no hemorrhages, no newly formed vessels.

of the aortic arch. The origins of the right innominate and left subclavian arteries are well identified. The origin of the left common carotid is not identified. Both subclavian and part of the origin of the vertebral arteries are not seen. Several large scapular and subscapular branches are seen suggesting blockage of the arteries at these levels (Fig. 12). Vectogram was read as within normal limits (Fig. 13).

The patient was discharged to be followed at the cardiac clinic at six months intervals. In the last cardiology clinic she was found to be a amenorrheic for the last four months and was referred to the prenatal clinics, where she is being followed up.

Discussion

Historical Review:

The first case of "pulseless disease" was probably recorded in 1839 by John Davy, in a 55-year old man, veteran from Waterloo, with absence of all pulses in the arms, neck and head. This disease was progressive and the autopsy report disclosed occlusion of several vessels arising from the aortic arch (12). Nothing was ever said again until 1856 when Savory reported his case of a

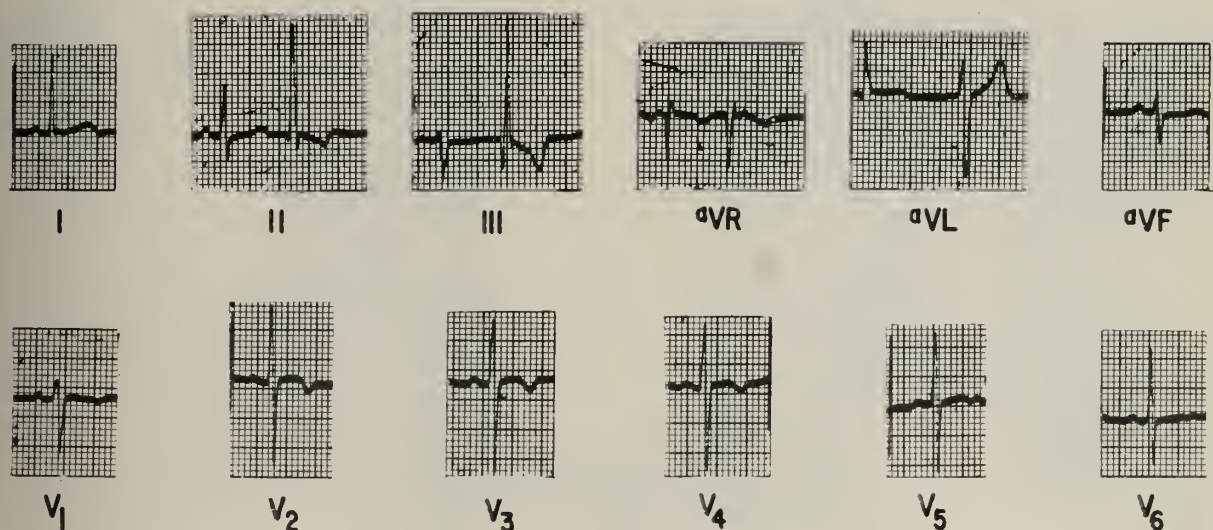


Fig. 9: J.R.M. Nov. 12, 1968. 12 Leads electrocardiogram showed non specific St- T wave abnormalities and frequent premature atrial beats with aberrant conduction.

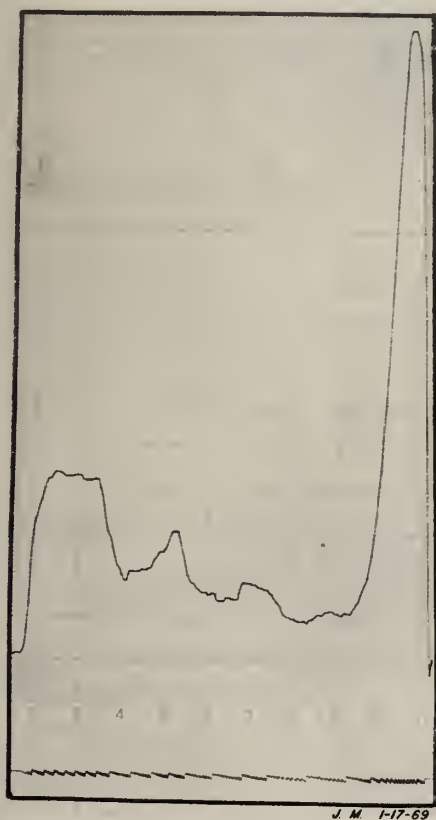


Fig. 10: J.M. 1-17-69. Serum electrophoresis of protein showed albumin within normal limits, increased Beta and a significant increased gamma globulin of the diffuse, polyclonal type.

young woman in whom the main arteries of both upper extremities (40) and of the left side of the neck were completely obliterated throughout. Kussmaul, in 1873, reported a similar case, in a 44-year old female with fainting spells and occluded cervical vessels (26).

In the years to follow, several authors reported cases in whom the syphilitic or arteriosclerotic etiology could not be ruled out. In 1908, Takayasu takes the credit for differentiating the arteritis which occurred with "predilection in young females," when in the Twelve Congress of the Japanese Ophthalmologic Society he reported "a case of strange changes in the central retinal vessels." (43)

Oonish, in the discussion that followed, concluded that he had encountered these ocular changes in a patient who had no pulse in the upper part of the body, reporting them that same year. Beneke, in 1925 (5) takes credit for reporting the autopsy stating that arteritis of the aorta was the main lesion, although several others had published their pathological report. Oota, in 1940 (36) confirmed these findings of the aorta, showing lesions even in the abdominal aorta, mesenteric vessels and pulmonary artery. The first case reported in the American literature was that of Elliot and his co-workers, in 1938, at the American Heart Association Meeting (14).

Terminology:

The aortic arch syndrome is an entity that has a common denominator obstruction of the larger vessels



Fig. 11: J.M.R. X Ray No. 21-89-00. X-Ray chest PA and lateral 3/12/69 showing cardiomegaly with cardiothoracic ratio (C.T.R.) of 12.8/24.2 centimeters associated with elongation of the aorta. The pulmonary vascularity is normally outlined and the lungs are clear.

arising from the aortic arch. The most common characteristic features are: (1) Malnutrition of the cranial half of the body, (2) increased blood pressure in the lower half of the body, (3) development of collaterals from the caudal half of the body. Ask-Upmark, (2, 3) Judge (22) have pointed to the following causes for the occlusion of these vessels: (1) Arteriosclerosis, (2) syphilitic aortitis, (3) trauma, (4) thrombotic processes, (5) collagen diseases, (6) congenital, (7) embolic, (8) neoplasia, (9) young female arteritis, (aortico subclaviocarotid arteritis, Takayasu's arteritis (Pulseless Disease).

Several names and eponyms have been proposed but none of them seem to be entirely adequate. The terms "pulseless disease," (42, 8, 37, 1, 13, 15) thrombotic obliteration of the branches of the aortic arch," (23) "thromboarteritis obliterans subclaviocarotica," (17) branchial arteritis (24) and "panarteritis brachiocephalica cardinalis" (18) are not proper at all because all of them fail to cover the entire clinical picture and some even may lead to wrong etiologic and anatomical deductions. The so used term "young female arteritis" must be abandoned, as the disease is not limited completely to their sex. The eponyms of Takayasu's disease and Martorell syndrome are also

subject to censorship as neither of those authors can be credited for the first description of the disease. We have to convene with Judge, *et al* (22) that as long as the etiology is unknown, in order to localize the disease and point to the accurate changes of the arteritis, the best suitable nomenclature is that of aortico-subclavio-carotid arteritis, accepting as a compromise the term Takayasu's arteritis.

Etiology:

There have been many speculations as to what is the etiology of the process. Earlier tuberculosis was suspected mainly because of the nature of the histology. Today there is no evidence for supporting such theory. Some have thought there was a congenital process as well as a rheumatic process. Still other has thought this was an entity like Buerger's disease, but all this has been mere theories and no definite proof for any has been attained. Many early works pointed to an allergic process, theory that has culminated in the latest speculations regarding this process in terms of an autoimmune disease (22). Hirsch, *et al* (19) has postulated this arteritis resembles systemic lupus erythematosus in several aspects. It is a chronic disease with periodic remissions and exacerbations, with elevated sedimenta-

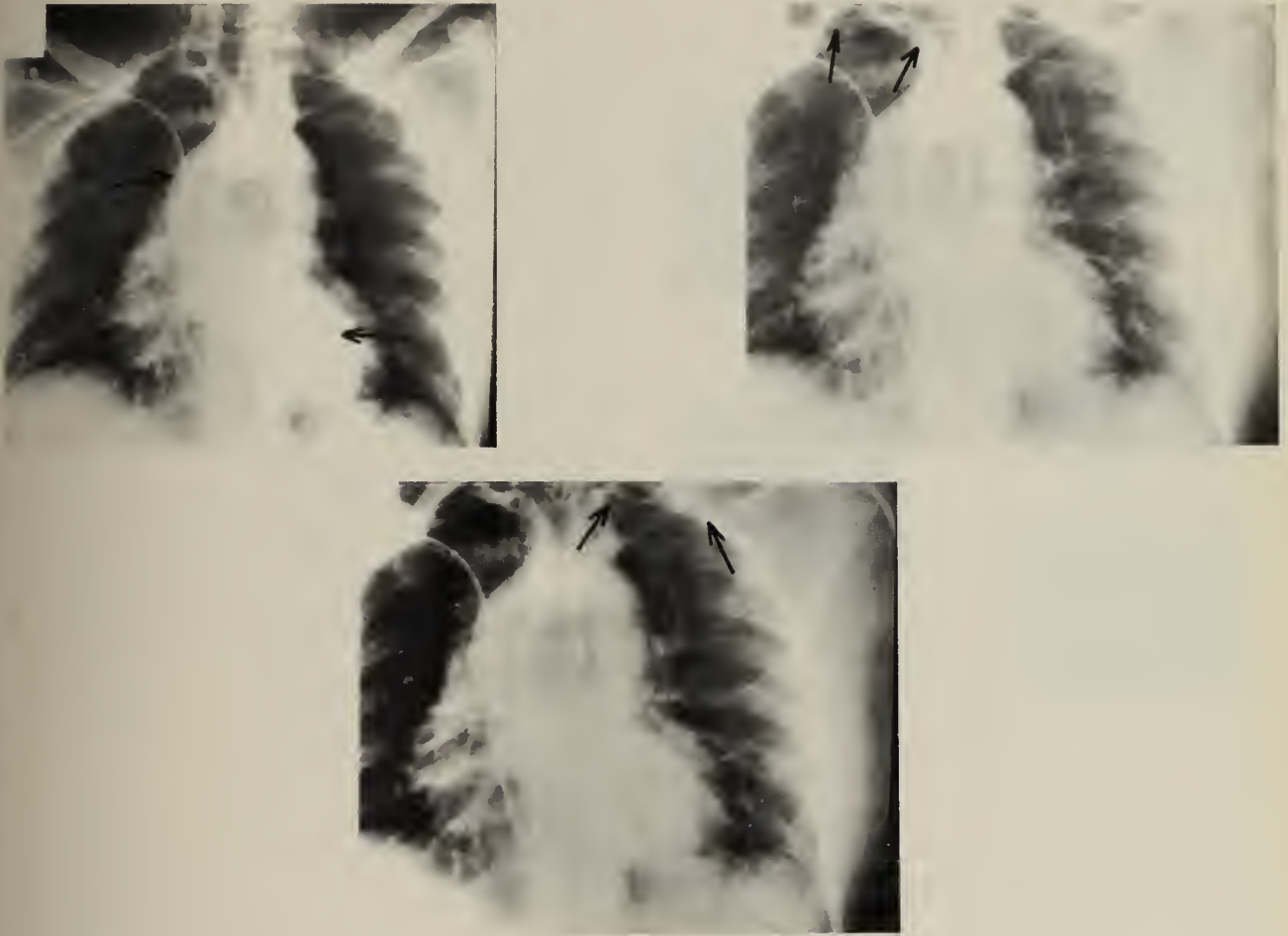


Fig. 12: Films above shows the Levophase of a right pulmonary arteriogram and show increased thickness of the left ventricular wall and a prominent thoracic aorta for the patient's age. The innominate artery is patent, as well as the right common carotid artery, but the right subclavian is markedly decreased in caliber. The left common carotid is not visualized. The left subclavian artery is patent, as well as the left vertebral. However, it decreases in caliber considerably as it becomes the left axillary artery and proceeds distally.

tion rate as a cardinal feature of the active phase, and with no microorganism ever cultured. It primarily affects women of the child-bearing age with some giving a history suggestive of rheumatic disease. However, with all the similarities of a collagen disease Hirsch, *et al*, using several parameters of immunopathic activity did not find circulating antibodies against human artery. Although no circulating antibodies have been yet found, still the autoimmune theory still is the most logical (25).

Pathology:

The primary lesion consists of an acute almost phlegmonous periarteritis (34).

The complete set of layers of the arterial wall are diffusely and irregularly thickened. This pathology is seen confined only to the aortic arch at times, but can be present in the entire vessel. The arteries commonly

involved are the common carotid, innominate and subclavians. There have been reports in literature where these changes have been described in the celiac, superior mesenteric, renal and iliac arteries, not forgetting instances in the pulmonary artery, as well as in the circle of Willis and the coronary arteries. The smaller arteries and arterioles are spared.

The inner surface of the involved vessel reveals irregular grayish white plaques. If a cross section is done this fibrous thickening is not only prominent in the intima, but can be seen in the media and adventitia. As a result of these changes the surface of the vessel wall becomes coarsely undulated and the artery is shortened in length. Nasu (34) believes that due to this shrunken state of the arteries, these patients assume a characteristic posture of dropping the head forward; and that the convulsion occurring

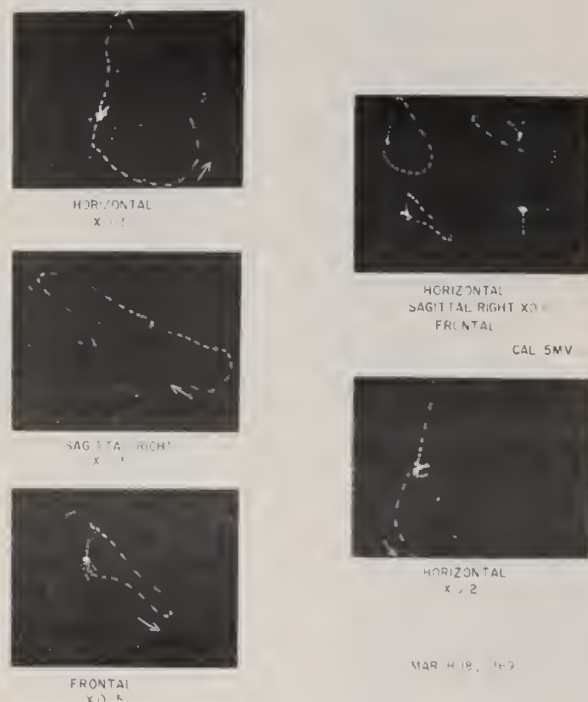


Fig. 13: J.M.R. March 18, 1969. Vectocardiogram was within normal limits.

when the head is backward is due to extension of these arteries aggravating the cerebral ischemia.

By histological examining, the principal lesions are the inflammatory changes occurring in the media and adventitia. Fresh inflammatory changes are rarely seen in the adventitial layer. Sometimes a perivascular infiltration of lymphocytes, plasma cells and mononuclear wandering cells are seen around the vasa vasorum (34).

The pathologic changes of the media are characterized, as exposed by Nasu (34) by the formation of granulomata. These can be of two types: those with coagulation necrosis accompanied by various types of giant cells, and the tuberculoid ones with Langhans giant cells. There is also a diffuse productive inflammation with lymphocytes and plasma cell infiltration (rarely accompanied by giant cells) and varying degrees of arteriosclerosis (24).

Close to the site of the changes in the medial and adventitial layers there is intimal thickening, this constituting the direct cause of the obliteration of the lumina of vessels. There is an increase in basophilic substance picked up by a positive periodic acid-Schiff, but findings suggestive of inflammation are rare. It is common to find thrombi formation in this thickened intima (9, 20, 32).

Signs and Symptoms:

The symptoms at the beginning are protean and depend upon the extent of the obliterative process and the adequacy of the recently created collateral circulation. The characteristic vascular sign is the absence of arterial pulsation in the neck, head and arms. Usually the axillary arteries, as well as internal and external carotids, are occluded in the process. These vessels and their collaterals can be demonstrated by percutaneous or retrograde aortography. The collateral circulation leads to vascular thrills in the neck, anomalous pulsation and rib notching. Blood pressure and oscillographic demonstration are not obtainable in the upper extremities but the pressure of the lower extremities is usually elevated.

The involvement of the cardiac structures is frequent and often there is a high pitched loud systolic murmur, heard best in the supraclavicular regions or at the base of the heart. These murmurs may be continuous or have a marked diastolic component simulating the bruit of a patent ductus arteriosus, aortic regurgitation or of a arteriovenous fistula.

Some authors have described instances of coronary involvement (35). Congestive heart failure is an ominous event and indicates the terminal stage of the entity, responding poorly to the usual management.

Due to the ischemia produced by the obliterative process there are some characteristic trophic changes, found with predominance in the upper half of the body (21). The perforation of the nasal septum is the most frequent sign, but loss of teeth and hair, plus ulcers on the lips and tip of the nose have also been described.

Other authors have described perforation of the drums. The muscles of (10) the upper extremities and of the face can appear wasted. Intermittent claudication of the arms can be seen as well as easy fatigability of the arms accompanied by feeling of coolness of upper extremities distally as well as proximally.

This obliterative phenomena brings central nervous system manifestations (38) such as dull headache, giddiness, syncope and loss of consciousness, mental impairment, hemiplegia, dizziness and vertigo and convulsive disorders. The syncopal episodes are typical fainting spells and are sometimes precipitated by rising, walking or changing position. The sensory changes that occur are paresthesias associated with weakness in one or the other upper extremity.

The ocular disturbances have been described intensively by Pinkham. These are due to chronic subnutri-

tion of the eyes brought about by the gradual occlusion of the innominate and left common carotid arteries (6).

The most frequent symptoms occurring is blurring of vision brought on by raising the head or on sitting up in bed. Other visual symptoms include gradual or sudden permanent loss of vision, pain the orbits, photopsia and visual hallucinations. Cataracts formation has also been described, mainly nuclear, according to Shimizu and Sano (42). Explained on the basis of impaired nutrition some have described too, arteriovenous anatomoses, atrophy of the iris and retinal hemorrhage. In the early stage the fundus is normal except for some arteriovenous anastomosis in the periphery. When these anastomoses develop along the veins, they become thinner and rosary like. If these anastomoses are formed around the papilla they give a wreath like appearance. The disk can also become atrophic. Sudden loss of vision temporarily and permanently have been recorded as well as optic atrophy.

The erythrocytic sedimentation rate has been described as being elevated when the disease is in active stage. The electrophoretic analysis of the serum proteins shows mainly increased gamma globulin and hypoalbuminemia. Birke points out that the increase in the gamma globulin is characteristic of fibrotic productive or reparative processes (7). Generalized symptoms such as anemia, weakness, fatigue, anorexia and weight loss (29, 30) are frequent findings.

Diagnosis:

Takayasu's arteritis has to be differentiated from other types of aortic arch syndrome. Age and sex that used to be of prime importance to many authors have lost their priority because many authors have described such findings in older women and in males. However, the disease has a preference for the younger age when females are in their full obstetrical capacity. This disease is progressive and in early stages of the arteritis there are no symptoms. The first sign of obstruction is the absence of pulse in the upper extremities with the absence of blood pressure also. This is the importance of vital signs being taken thoroughly and conscientiously. In the early stages of the disease there is an elevation of the sedimentation rate and so of the gamma globulin component of the proteins. Electrocardiogram, vectocardiogram and X ray of chest are non specific in their findings. They are complementary measures in a clinical complex.

The aortography is the only method that help us the most in delineating the extent and nature of the vascular involvement.

The absence of lupus erythematosus cells, syphilis, tuberculosis and arteriosclerosis in the presence of absence of pulse, elevated sedimentation rate and electrophoretic pattern, with hypergamma globulin were of prime importance in reaching a definite conclusion and ruling out some diseases.

Being a disease thought to be predominantly of "young females" we are amazed to encounter no reports dealing with its management during pregnancy. Reviewing the literature as back as 1941 we have found 13 cases of Takayasu's disease in patients who were pregnant before and after the diagnosis of such entity (2, 3, 9, 32, 6, 7, 45). In all these cases little is said about the prenatal care or any complication arising during pregnancy or labor. This silence makes us believe that with the joint effort between the internist and the obstetrician, these patients traverse pregnancy successfully.

This disease has its protean clinical manifestation and we believe a good history and physical examination will enlighten, as always, the future management. The importance of vital signs checked by the examiner is stressed. Practically always we have a young female who, in her past history, has had episodes of fever of unknown origin, or arthralgias accompanied by the absence of pulse and blood pressure in the upper extremities.

This disease, being of a progressive nature, is seen in different stages. The most common is the manifestation of early signs of ischemia in the upper part of the trunk, and the absence of pulse and blood pressure.

These patients should be classified according to their functional capacity; degrees of ischemic signs in the upper trunk and signs of cardiac derangement. As cardiac patients, the adopted functional classification of the New York Heart Association has worked for us in making a future prognosis. Our cases present minimal manifestation of the disease and did not present any sign of cardiac failure or ocular signs, so we classified them as Class I, believing that if we took the same measures as for Class I cardiac patients, we would elaborate a plan for their future management.

After the patients 32nd week of gestation they passed the overloading period without complications. They were placed in low salt diet and weekly visits to the internist and obstetrician were instituted. It was our belief that if we could control anemia, infections, over-exertion and stress from (47) thereafter, the patients will have an excellent chance of

having normal deliveries. Hypervolemia and weight were controlled and the patients had no further dyspnea or headaches. Labor was uneventful, with no signs of cardiac failure. In one case the anesthesia was pudendal block, as no epidural anesthesia could be given, because of lack of control of blood pressure. After delivery, the patients were treated as any other Class I cardiac and were discharged home after an uneventful post partum period.

Treatment:

As this disease has an unknown etiology and many aspects of its cause are not clear yet, it is of prime importance to establish a diagnosis with certainty, before starting any treatment. Steroids has been used with some success. Hirsh (19) states that the sedimentation rate appears to mirror the activity of the disease and that when elevated, it would justify anti-inflammatory therapy. There is no rationale for steroid treatment in cases with no signs of activity. We mean by this, normal sedimentation rate and non progression of symptoms.

Vasodilators have been of help in providing symptomatic relief, specially when they are used in conjunction with steroid as stated by the French literature. The success of anticoagulation is not well established. Nevertheless, anticoagulation has been used with the idea of preventing thrombosis in the already narrowed arteries.

Sometimes the surgeon has come in our assistance to avoid catastrophic blockage of carotid vessels. Patients selected for surgery are those with transitory symptoms when the progress of the disease is arrested naturally, or with the aid of steroids. Endoarterectomies or carotid bypass grafts from the ascending aorta have been used in these cases with success, by some surgeons (11, 46).

Treatment in pregnancy should depend (1) in the certainty of the diagnosis, (2) the presence of elevated sedimentation rate, (3) the presence of progression of symptoms. As the methods in use for therapy carry risks, these should be reserved to cases with impending catastrophic damage. Steroids should be used with the same reserve as in other diseases and anticoagulation, if used, should be carried out with Heparin, since it does not pass the placental barrier (27, 46). In this way the fetus is guarded from having dangerous hemorrhages. Surgery should be offered to cases where the cerebral blood flow is so compromised that fear for the life of both mother and child is present. We believe that a fair trial with a medical regime should be given, utilizing the

same criteria used for surgery in a cardiac patient (45). We should bear in mind that surgery can be offered with success at any time in pregnancy, but that the ideal time is before the 24th week and that the patient seen after this time should wait until after delivery.

Summary

Two cases of Takayasu's Arteritis or the so called "pulseless disease" are reported, diagnosed at the 32nd and 39th weeks of gestation. Minimal symptoms of vascular insufficiency dominated the clinical picture with increased sedimentation rate. Being a disease of young females and occurring in an age when pregnancy occurs, we were surprised to find in the review of the literature only very few aspects of the management of prenatal care and labor in these cases. The silence of the literature in this respect makes us believe that this entity usually ends successfully, (both for mother and child) the final outcome depending on the degree of involvement of the arteries.

Our proven cases of Takayasu's Arteritis, diagnosed after delivery by a retrograde aortogram, have helped us in establishing a combined medical and obstetrical regime, so as to help women with this progressive disease.

The entity is reviewed pointing out the resemblance with other immunopathic processes and some aspects of its therapeutic parameters, as related to pregnancy, are discussed.

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ACUTE TRIFASCICULAR BLOCK – A REPORT OF FOUR CASES AND A REVIEW OF THE LITERATURE

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The human intraventricular conducting system operates as a trifascicular system. The depolarization of the ventricles occurs through the right bundle and the anterior and posterior divisions of the left bundle branch. These divisions are affected by several processes including coronary disease, myocarditis, Lev's disease, Lenegre's disease, cardiomyopathies, ostium primum defects and a familial autosomal dominant heritable disorder, as recently reported.

We are reporting four cases of acute trifascicular block related to coronary disease. They are 1) permanent complete right bundle branch block (C.R.B.B.B.) and left anterior hemiblock (L.A.H.) with intermittent posterior hemiblock (L.P.H.); 2) intermittent R.B.B.B., L.P.H. and L.A.H.; 3) intermittent R.B.B.B., L.A.H. and L.P.H.; 4) permanent L.A.H., L.P.H. and intermittent R.B.B.B.

The literature, prognosis and treatment are reviewed.

Material and Methods

Case 1

This was the first University Hospital admission for this 83-year old female with a history of bronchial asthma since age 30. Since that time she has been complaining of some dyspnea on exertion. She did relatively well, until three years prior to this admission when she developed dyspnea on exertion, paroxysmal nocturnal dyspnea and two pillows orthopnea. At that time, she was told to be hypertensive. She was digitalized and started on hypertensive treatment. Ten days prior to admission she developed a severe cough, four pillows orthopnea and then was referred to the University Hospital for further evaluation and treatment. She denied a previous history of chest pain, leg edema and hemoptysis.

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At the emergency room, she was digitalized and Salyrgan was given with relief of her symptomatology. There she developed severe intermittent epigastric pain radiating to the left hemithorax and at the same time nausea and sweating appeared. She was admitted for further evaluation and treatment.

Physical examination on admission revealed a blood pressure of 160/80, a pulse rate of 80 per minute and a temperature of 36° C. She was a well developed female who was in acute distress. The neck showed engorgement of the veins at a body angle of 45°. The chest examination showed an increase in the antero-posterior diameter, the lungs were hyperresonant to percussion and there were moist rales in both bases. The apex impulse was at the sixth intercostal space and 3 to 4 cms outside the midclavicular line. There was a grade I/VI systolic murmur at the apex, and S3 and S4 gallops were heard. The liver edge was 4 cms below the right costal margin with a total span of 18 cms. The extremities did not show edema or a Homan's sign. Laboratory studies were all within normal limits except the transaminases that were 50, 64, 82 and 29 units on consecutive days. The chest x-rays showed cardiomegaly and venous engorgement compatible with heart failure. The patient was hospitalized for 22 days, and she was discharged on digoxin, lasix and potassium chloride. She has been doing relatively well with the above therapy.

An electrocardiogram done on May 9, 1969 at 4:00 pm (Fig. 1a) showed an axis in the frontal plane of -60° (anterior hemiblock) and a complete right bundle branch block (C.R.B.B.B.), and the ST segments were depressed from V₁ - V₆. Two hours later the electrocardiogram (Fig. 1b) showed an axis of around -60° (anterior hemiblock), C.R.B.B.B. and giant T waves in V₄ - V₅. An electrocardiogram done at 7:00 pm on the day of admission (Fig. 1c) showed an axis in the frontal plane of +120° (posterior hemiblock) C.R.B.B.B. and prominent peaked T waves in V₂ and V₅. The electrocardiogram done on May 13, 1969 (Fig. 1d) again showed an axis of -60° (anterior hemiblock) and C.R.B.B.B., and the P-R interval was 0.20 seconds, again changes compatible with trifascicular block.

A vectorcardiogram done on June 20, 1969 (Fig. 5a) showed an axis in the frontal plane of -70° with counterclockwise rotation (anterior hemiblock), and terminal delay to the right and superiorly compatible with right bundle branch block. The QRS loops were oriented superiorly and anteriorly.

Case 2

This was the second University Hospital admission for this 52-year old male who was doing well until one month

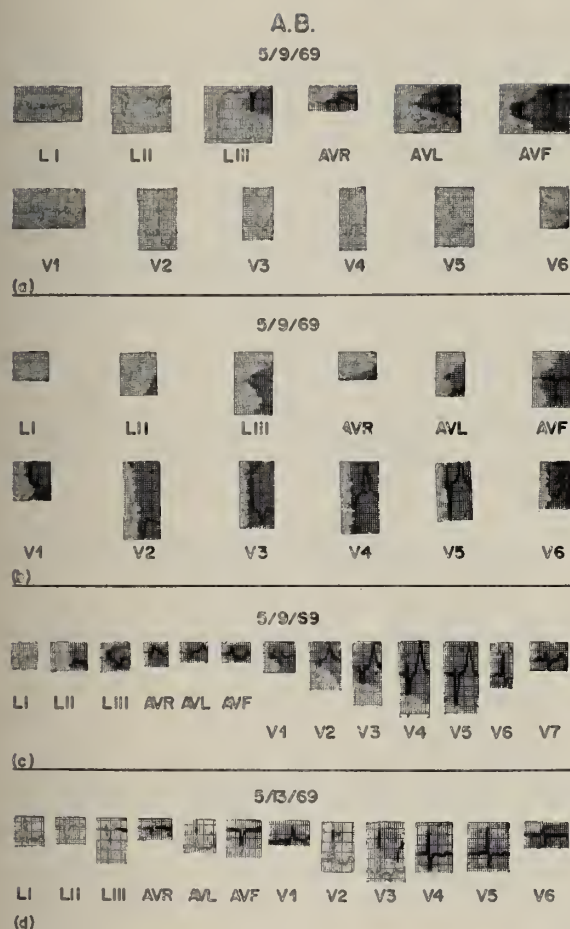


Fig. 1: a) Electrocardiogram done on May 9, 1969 at 4:00 p.m.; b) Electrocardiogram done on May 9, 1969 at 6:00 p.m.; c) Electrocardiogram done on May 9, 1969 at 7:00 p.m.; d) Electrocardiogram done on May 13, 1969.

prior to this admission (March 12, 1971) when he developed pain in the left hemithorax with radiation to the back. The pain was not accompanied by nausea, vomiting or diaphoresis. It lasted for about 15 minutes. He remained at home without medical treatment.

About five days prior to his admission he developed severe precordial pain, dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, palpitations and progressive leg edema. He denied a history of hypertension or diabetes but had been a chronic smoker for about 30 years. He was referred for evaluation and treatment.

Physical examination on admission showed a blood pressure of 110/70, a pulse rate of 100 per minute and a temperature of 37° C. There was neck vein distension at 45° and prominent a waves. There were lenticular opacities, retinal A-V nicking, and the arterioles showed a silver wire appearance. There was a mild increase in the antero-posterior diameter of the chest and there were moist rales in both bases. The heart examination revealed atrial and ventricular gallops. The extremities showed a grade II pitting edema.

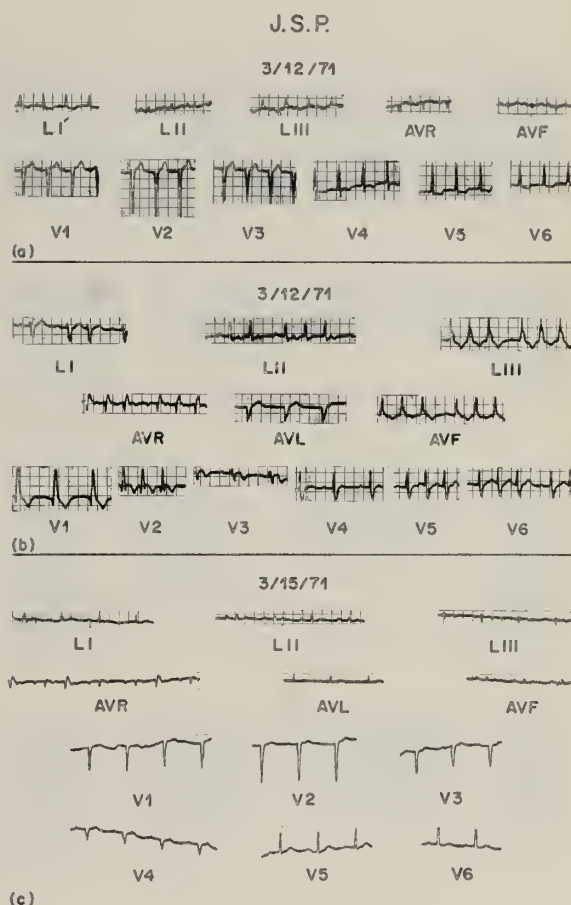


Fig. 2: a) Electrocardiogram done on March 12, 1971 at 9:00 a.m.; b) Electrocardiogram done on March 12, 1971 at 11:00 a.m.; c) Electrocardiogram done on March 15, 1971.

Laboratory work-up showed normal values for hemoglobin, electrolytes, BUN, creatinine, cholesterol, total lipids, uric acid and the urinalysis. The fasting blood sugar was 150 mgs percent. The chest x-ray on admission demonstrated cardiomegaly and findings compatible with congestive heart failure. An electrocardiogram done on March 12, 1971 at 9:00 am showed an axis in the frontal plane of about 0°, poor progression of the R waves in the right precordial leads, a P-R interval of 0.16 seconds and T wave changes compatible with ischemia (Fig. 2a).

A second electrocardiogram done on March 12, 1971 at 11:00 am showed a dramatic change in axis to the right (+130°) (posterior hemiblock), a complete right bundle branch block, a P-R interval of 0.22 second (delay conduction through the anterior division of the left bundle) and changes of an acute anteroapical myocardial infarct (Q waves in V₁, V₂) (Fig. 2b). The above findings are compatible with an acute trifascicular block. Episodes of ectopic atrial tachycardia (3:1, 4:3, 2:1 A-V block) were also present.

An electrocardiogram done three days later, on March 15, 1971, showed an axis of +60° and a P-R interval of 0.22 se-

conds. Three right bundle branch block type beats similar to those of the previous tracings were also present in lead AVR. An atrial tachycardia with 2:1 block was present and findings compatible with an anteroseptal myocardial infarct (Fig. 2c). A vectorcardiogram done on the same day was compatible with an anteroseptal and lateral myocardial infarct (Fig. 5d). The patient was admitted to the hospital and anticoagulated with heparin. When he developed electrocardiographic findings of trifascicular block, a demand intravenous pacemaker was inserted and maintained for about 12 days without complications. He was discharged after 30 days in the hospital to be followed at the Cardiology Clinic.

Case 3

This was the first University Hospital admission for this 77-year old negro male who was doing well until one year prior to admission when he developed severe substernal pain related to exercise and alleviated by rest. This pain increased in intensity and frequency and in the last two months it was accompanied by palpitations, orthopnea and paroxysmal nocturnal dyspnea. On the day of admission he developed severe chest pain accompanied by severe dyspnea at rest, dizziness and diaphoresis. He was referred to the University Hospital for evaluation and treatment. He denied a history of hypertension or diabetes, but he was a chronic smoker for the last 50 years.

Physical examination on admission, January 25, 1971, showed a blood pressure of 120/90, a pulse rate of 88 per minute and a temperature of 35° C. The neck showed venous distention at 45° and there were bilateral lens opacities. The lungs revealed bilateral moist rales in the bases. There was a grade 1/V1 systolic murmur at the apex and an atrial gallop. The extremities showed a grade 1 pitting edema. The patient was admitted to the hospital and digoxin, diuretics and heparin were administered and a demand intravenous pacemaker was inserted with relief of his symptomatology. He was hospitalized until March 4, 1971. During that time he developed several episodes of chest pain and he went into moderate to severe heart failure. He was discharged taking digoxin, lasix and coumadin and at the present time is doing relatively well.

Laboratory studies showed normal values for hemoglobin, BUN, creatinine, SGOT, SGPT, LDH, urinalysis, electrolytes, cholesterol, total proteins, albumin and globulin. The fasting blood sugar was 200 mgs percent on admission and 100 mgs percent on discharge. His chest x-ray showed cardiomegaly and findings compatible with congestive heart failure, that improved with therapy.

An electrocardiogram done on January 24, 1971 showed an axis of -60° (anterior hemiblock) and elevation of ST segments from leads V₁ -V₄: There was loss of septal forces from V₁ -V₃. One premature beat in L₂ showed a more marked degree of left axis deviation (Fig. 3a).

The electrocardiogram performed on January 26, 1971 at 8:00 am showed an axis of -90° (a more marked degree of anterior hemiblock). There were elevation of the ST segments from leads V₁ -V₆ (Fig. 3b).

An electrocardiogram done on the same day at 10:00 am during severe chest pain showed anterior hemiblock, complete right bundle branch block (C.R.B.B.B.) and elevation of the ST segment from leads V₁ -V₆. Q waves were present in leads V₃ -V₅ (Fig. 3c). The electrocardiogram done later

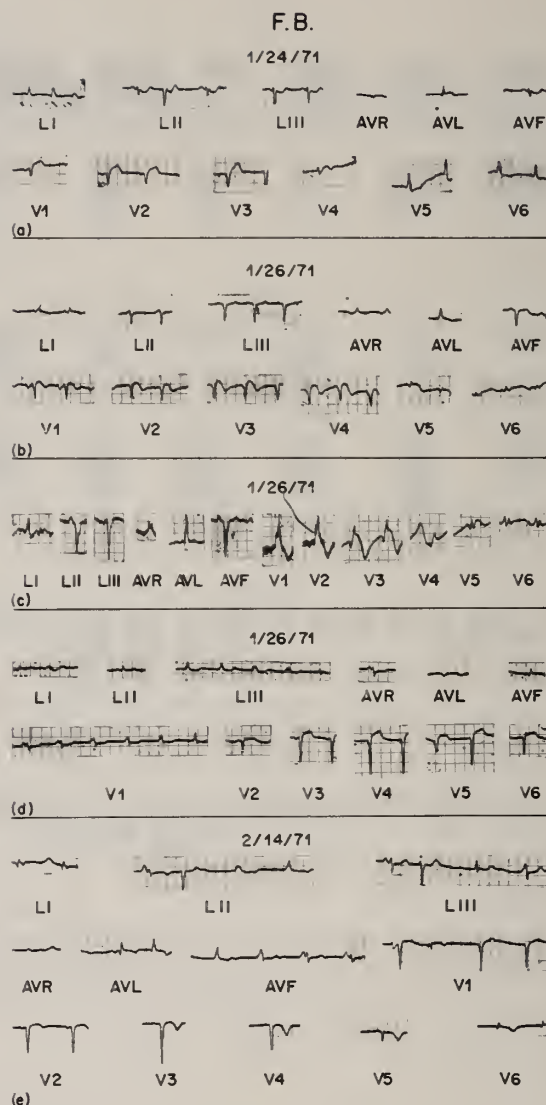


Fig. 3: a) Electrocardiogram done on January 24, 1971; b) Electrocardiogram done on January 26, 1971 at 8:00 a.m.; c) Electrocardiogram done on January 26, 1971 at 10:00 a.m.; d) Electrocardiogram done on February 14, 1971.

at 1:00 pm on the same day showed an axis of +100° (posterior hemiblock), A-V dissociation and elevation of the ST segment from leads V₂ -V₆ (Fig. 3d).

The electrocardiogram done on February 14, 1971 showed an axis around +80°, A-V dissociation, ST segment elevation from V₁ -V₆ and T wave inversion in L₂, AVL and V₁ -V₆. One beat in L₂, L₃ showed left axis deviation.

The vectorcardiogram performed on February 18, 1971 showed an axis in the frontal plane of -70° with clockwise rotation of the QRS loop, and the findings were compatible with an anterolateral myocardial infarction. The ST-T loop

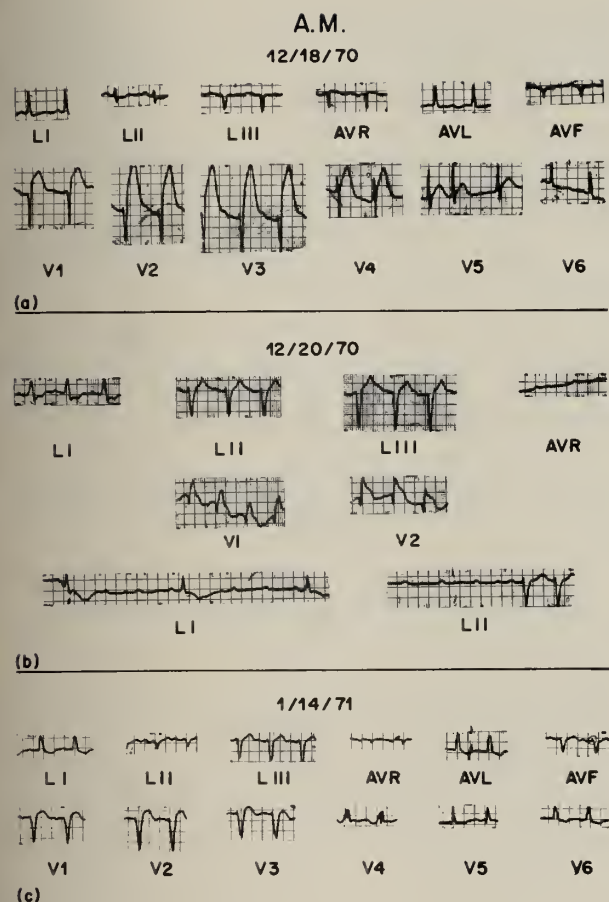


Fig. 4: a) Electrocardiogram done on December 18, 1970; b) Electrocardiogram done on December 20, 1970; c) Electrocardiogram done on January 14, 1971.

in the horizontal plane was located to the right. The QRS loop was superior and posteriorly located (Fig. 5c).

Case 4

This was the first University Hospital admission, (December 18, 1971), for this 58-year old male with a history of hypertension for the last seven years. He had been receiving Serpasil and diuretics, and his blood pressure had been under control.

About two months before admission he started to have precordial pain radiating to the left arm. This pain was increased by exercise and was alleviated by nitroglycerin. On the day of admission he developed severe chest pain accompanied by dizzy spells. He was referred to the emergency room and admitted for further evaluation and treatment. He denied a history of orthopnea, paroxysmal nocturnal dyspnea, pitting edema or diabetes.

Physical examination on admission showed a blood pressure of 160/110 and a pulse rate of 100 per minute. He was a well developed, obese male complaining of severe chest pain. The pupils were equal and the retinal vessels showed A-V nicking

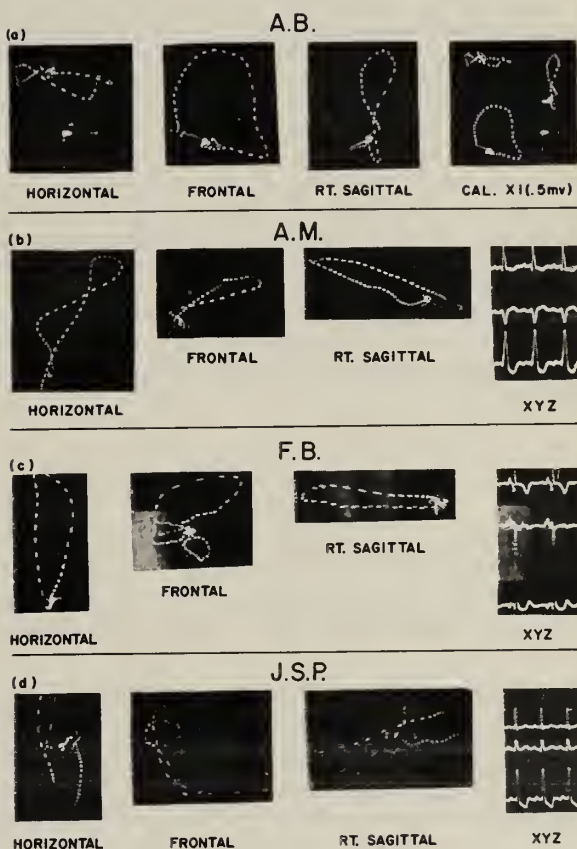


Fig. 5: a) (Case I) Frank vectorcardiogram done on June 20, 1969; b) (Case IV) Frank vectorcardiogram done on February 15, 1971; c) (Case III) Frank vectorcardiogram done on February 18, 1971; d) (Case II) Frank vectorcardiogram done on March 15, 1971.

and marked vasoconstriction. The neck veins were not engorged. The lungs were clear to auscultation and percussion. The heart examination revealed a grade II/VI systolic murmur at the apex, and filling and atrial gallops were heard. The abdomen and the extremities were within normal limits.

The patient was admitted to University Hospital where he received oxygen, heparin and digitalis. Laboratory studies showed normal values for the blood sugar, BUN, creatinine, hemoglobin, cholesterol, total lipids, urinalysis, and liver profile. The chest x-ray showed cardiomegaly and venous engorgement, findings compatible with heart failure.

The electrocardiogram on admission showed an axis of -30° , a P-R interval of 0.18 seconds and giant T waves from V_1 - V_4 , and marked ST segment elevations (Fig. 4a). He did relatively well until December 20, 1970 when he developed severe chest pain and an Adams-Stokes episode. The electrocardiogram at that time showed an axis of -80° , (anterior hemiblock) a P-R interval of 0.22 seconds (delay conduction through the posterior division of the left bundle) and complete right bundle branch block (C.R.B.B.B.). Strips of

leads L_1 and L_2 showed episodes of complete A-V block (Fig. 4b). An intravenous pacemaker was inserted, and the patient was kept in the hospital and did well for about 40 days. An electrocardiogram done on January 14, 1971 showed an axis in the frontal plane of -50° , a P-R interval of 0.20 seconds, ST segment elevation and coving from V_5 - V_6 (Fig. 4c).

The vectorcardiogram done on January 15, 1971 demonstrated on axis in the frontal plane of -40° and the QRS loop rotating counterclockwise (anterior hemiblock). There was a terminal delay. The QRS loop was located posteriorly and superiorly. The efferent loop was displaced to the right. An ST vector was present (Fig. 5b).

The patient was transferred to the nursing home, but one day later he developed severe chest pain and was re-admitted to the hospital in cardiogenic shock, and died one day after the admission.

Discussion

The human left bundle branch system can really operate as a bifascicular system and the whole intraventricular conducting system as a trifascicular system (1, 2).

Among the recognized causes of trifascicular block are coronary artery disease, calcific aortic valvular stenosis with fibrocalcereous penetration of the membranous septum, Lenegre's disease, Lev's disease, cardiomyopathies, Chagasic (1, 2) and rheumatic carditis (3) and other non-specific myocarditis (4, 5). It has also been described in ostium primum defects (2), and most recently as a familial autosomal dominant heritable disorder (6).

The eight possibilities of intraventricular trifascicular blocks are the following: 1) right bundle branch block (R.B.B.B.) with intermittent left anterior hemiblock (L.A.H.) and left posterior hemiblock (L.P.H.); 2) R.B.B.B., L.A.H. and L.P.H. all permanent (trifascicular, complete heart block); 3) permanent R.B.B.B. and L.P.H. and L.P.H. with intermittent L.A.H.; 4) permanent R.B.B.B. and L.A.H. with intermittent L.P.H.; 5) permanent L.A.H. and L.P.H. with intermittent R.B.B.B.; 6) permanent L.P.H. with intermittent R.B.B.B. and L.A.H.; 7) permanent L.A.H. with intermittent R.B.B.B. and L.P.H.; 8) R.B.B.B., L.A.H. and L.P.H. all intermittent (1, 2, 7, 8).

In reviewing, our first case (Table I), was an elderly female patient who was digitalized three years ago because of heart failure. The electrocardiogram done on admission showed an axis of -60° and counterclockwise rotation of the QRS loop in the frontal loop (L.A.H.). During severe chest pain episodes, she developed a marked change in the axis to $+120^\circ$ (L.P.H.). Later, the L.P.H. disappeared and the L.A.H. plus the C.R.B.

B.B. persisted. This is an example of C.R.B.B.B. and L.A.H. with intermittent L.P.H.

Our second case (Table I) was a diabetic, chronic smoker with coronary artery disease who was having episodes of severe chest pain and who also went into heart failure. The first electrocardiogram done on March 12, 1971 only showed poor progression of the R waves and T wave changes compatible with ischemia; the axis was 0° in the frontal plane. The second electrocardiogram done showed a marked change in axis to $+130^\circ$ (L.P.H.) C.R.B.B.B. and a P-R interval of 0.22 seconds. The patient developed episodes of atrial tachycardia with different degrees of A-V block in the anterior division of the left bundle. In this case a pacemaker was implanted. This is an example of intermittent R.B.B.B., L.P.H. and L.A.H. The vectorcardiogram was compatible with an anteroseptal myocardial infarction.

The third case was a male diabetic chronic smoker (Table I) who went into heart failure. The electrocardiogram done on January 24, 1971 showed different degrees of L.A.H. Later, during an episode of severe chest pain he developed C.R.B.B.B. with L.A.H., that changed to L.P.H. and A-V dissociation. This is an example of intermittent L.A.H., L.P.H. and R.B.B.B. In this case a pacemaker was implanted. The vectorcardiogram was compatible with an anterolateral myocardial infarction.

The fourth case was a hypertensive patient with a history of chest pain and heart failure. The electrocardiogram on admission showed an axis of -30° (L.A.H.), and giant T waves. The electrocardiogram performed when he developed the attacks of Adams-Stokes showed an axis of -80° (a greater degree of L.A.H.) and a P-R interval of 0.22 seconds (a delay in conduction through the posterior division of the left bundle) and C.R.B.B.B. The last electrocardiogram showed a L.A.H. and a P-R interval of 0.20 seconds. This is an example of permanent L.A.H., intermittent R.B.B.B. and delayed conduction through the posterior division. A demand pacemaker was implanted. The vectorcardiogram showed L.A.H. and anteroseptal myocardial infarction.

The main cause of R.B.B.B. with L.A.H. or L.P.H. and trifascicular block is undoubtedly coronary heart disease (1, 2), especially when there is some obstruction in the anterior descending coronary artery, with or without anteroseptal or anterolateral myocardial infarction. This is because the right bundle branch and the anterior division of the left bundle run close together in the interventricular septum, and share a

TABLE I: CLINICAL DATA FOR THE 4 PATIENTS WITH ACUTE TRIFASCICULAR BLOCK

Case No.	Age	A QRS	Kongest P-R Interval	Type of A-V Block	Other Conduction Disturbances	Location of Myocardial Infarction	Outcome
I	83	-60°; +120°	0.20 sec.	---	*C.R.B.B.B. +L.A.H.; ‡ L.P.H.	---	Alive 95 months)
II	52	0°; +130° +60°	0.22 sec.	3:1; 4:3 2:1 A-V block	C.R.B.B.B. L.A.H.; L.P.H.	Anteroseptal	Pacer (Alive 6 months)
III	77	-60°; -90° +100°	0.18 sec.	A-V dissociation	C.R.B.B.B. L.A.H.; L.P.H.	Anteroseptal	Pacer (Alive 6 months)
IV	58	-30°; -80° -50°	0.22 sec.	A-V Block	C.R.B.B.B. L.A.H.; L.P.H.	Anteroseptal	Pacer (Dead)

* C.R.B.B.B. = Complete right bundle branch block

+ L.A.H. = Left anterior hemiblock

‡ L.P.H. = Left posterior hemiblock

common blood supply from septal branches of the left anterior descending coronary artery (2, 9). The posterior division of the left bundle has a different blood supply (from both coronary arteries) (2, 9). Right bundle branch block with right axis deviation (R.B.B.B. + L.P.H.) is therefore even more dangerous in acute myocardial infarction, because a greater part of the septum must be involved and there should be a more generalized myocardial damage (2, 7, 8, 10, 11).

Several authors have reported that bundle branch block with abnormal left axis deviation precedes the development of symptomatic A-V block (7, 8, 10, 11, 12). They have attributed the abnormal left axis deviation to a block in the anterior division of the left bundle. This pattern has been interpreted as a form of bilateral bundle branch block (13, 14). Less emphasis has been placed on the fact that C.R.B.B.B. with right axis deviation can also be a precursor of symptomatic A-V conduction disturbances (2, 10, 11, 12, 15). Of course, it is well recognized that C.R.B.B.B. with right axis deviation frequently occurs in patients with right ventricular hypertrophy pulmonary diseases, extremely vertical hearts or massive lateral wall infarction. Several authors have stressed that the association of C.R.B.B.B. and right axis deviation, in the absence of the complicating factors mentioned above, represents a simultaneous conduction block in the right branch and in the posterior division of the left branch (1, 2, 10, 11, 12). This diagnosis is strengthened by the appearance of advanced A-V block (2, 11, 12). It has been empha-

sized that in the presence of a simultaneous block in the right branch and in the inferior division of the left bundle an A-V block most probably indicates that there is conduction problems (incomplete block) through the anterior division of the left bundle and in the presence of R.B.B.B. and L.A.H., an A-V block indicates impedance of conduction (incomplete block) through the inferior division of the left bundle (2, 11, 12).

Castellanos reported in 1970 five cases of patients with acute trifascicular block, and he pointed out the high incidence of A-V block and mortality in these patients, because C.R.B.B.B. + L.P.H. presupposes significant septal and bundle branch lesion due to a massive anterior wall infarction (11). Several authors have reported that the appearance of A-V block in acute infarction is a bad prognostic sign, because it suggests a bilateral bundle branch block (2, 14, 15, 16). Three of our patients developed A-V block (Table I) and they were treated with a pacemaker, although we think that in all patients with acute trifascicular block a temporary intravenous pacemaker should be inserted.

Rosselot *et al* reported ten cases of trifascicular block of which three were related to acute myocardial infarction and he reported a high incidence of Adams-Stokes attacks that were corrected by pacing, a low incidence of coronary heart disease as a causal factor, and a tendency to regain A-V conduction after pacemaker placement (16).

Roos and Dunning (18) reported ten patients with acute anteroseptal myocardial infarction associated with

right bundle branch block and obvious left axis deviation. He reported a high mortality in those patients mainly due to cardiogenic shock. Frequent complications were sudden complete heart block (five patients) and ventricular asystole (four patients). He stressed the use of a demand pacemaker in those patients that developed C.R.B.B.B. with left or right axis deviation after an acute myocardial infarction.

Scanlon, Pryor and Blount (19) reported 209 cases of partial bilateral bundle branch blocks. These included patients with right bundle branch block and either anterior or inferior intraventricular block. It was pointed out by them that the majority of patients were cases of coronary disease and that the incidence of complete heart block was 14.4 percent. The incidence of complete heart block in patients with C.R.B.B.B. + L.A.H. was around 13 percent, while the incidence of complete heart block in patients with C.R.B.B.B. + L.P.H. was 21 percent. This observation correlates well with our experience and other observers, because C.R.B.B.B. + L.P.H. usually mean more extensive disease.

Of our four patients (Table I) one died in cardiogenic shock when he was waiting for a permanent pacemaker, and the other three are doing well. None of the three have required a permanent pacemaker although it is our practice, at the present time, to place a temporary demand pacemaker when a patient with coronary disease develops a pattern of acute trifascicular block, because of the high incidence of complete A-V block, asystole and Adams-Stokes attacks.

It is our belief that all patients who develop acute trifascicular block after a myocardial infarction would be benefited by a temporary endocardial pacemaker as a preventive measure.

Resumen

El sistema de conducción intraventricular opera como un sistema trifascicular. La depolarización ventricular ocurre a través del fascículo derecho y la rama anterior y posterior del fascículo izquierdo. Estos fascículos y ramas pueden ser afectados por diferentes procesos patológicos, como enfermedades de las coronarias, miocarditis, enfermedad de Lev, enfermedad de Lenégre, cardiomiopatías, defectos atrio-ventriculares y como un proceso hereditario.

Reportamos cuatro casos de bloqueo trifascicular agudo, relacionado con enfermedad coronaria. Estos son:

1. Bloqueo permanente del fascículo derecho y de la rama anterior del fascículo izquierdo, con bloqueo inter-

mitente de la división posterior del fascículo izquierdo.

2. Bloqueo intermitente del fascículo derecho y de la rama anterior y posterior del fascículo izquierdo (2x).

3. Bloqueo permanente de la rama anterior y posterior del fascículo derecho.

Se repasa la literatura, pronóstico y tratamiento de los bloqueos trifasciculares agudos.

Acknowledgment

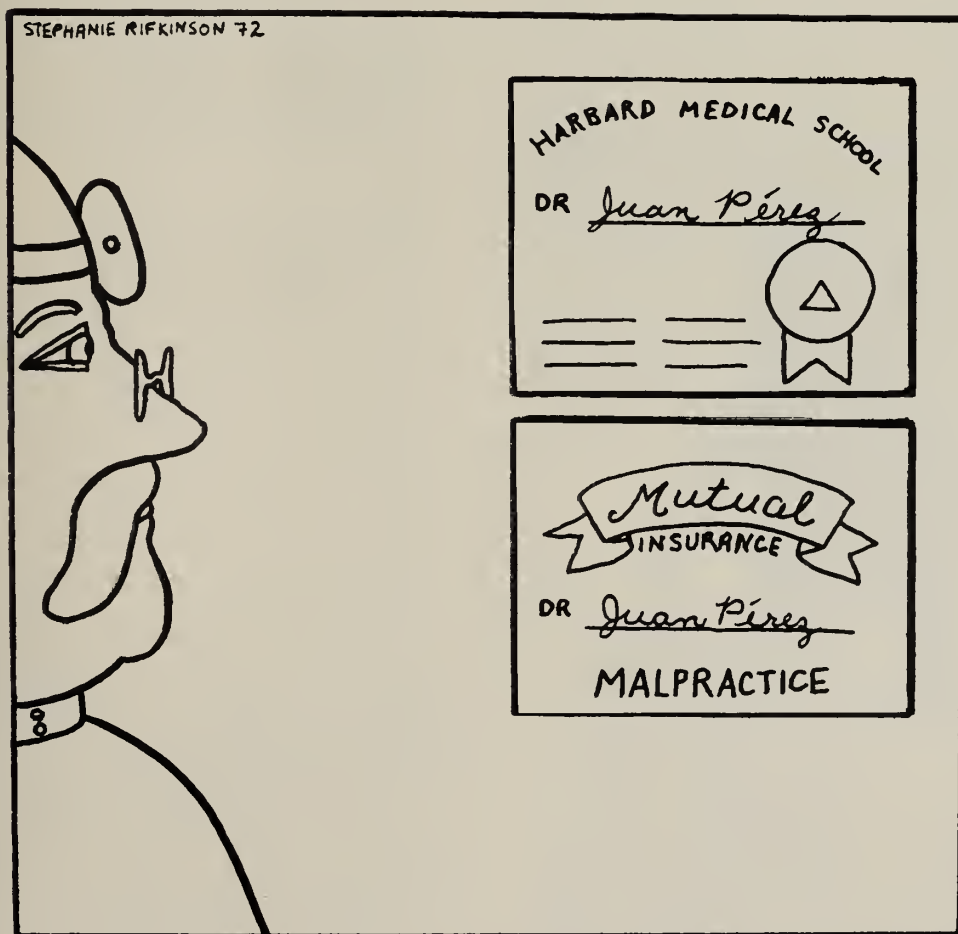
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HYPERLIPOPROTEINEMIC TYPES AMONG PUERTO RICANS: A PROGRESS REPORT

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The importance of preventive therapy for atherosclerosis has gained widespread recognition as evidenced by strong public interest in low-cholesterol and low-fat diets, and exercise programs. Physicians generally applaud and support these mass trends.

Pin-pointing of individuals who are genetically disposed to lipid-related vascular problems, and placing them on specific preventive regimes tailored to their particular syndromes, however, is potentially far more beneficial. Diagnostic laboratory tests for such pin-pointing involves four observations, namely serum lipoprotein electrophoresis, serum cholesterol, and triglyceride determinations, and observation of serum turbidity. These tests arose out of work done at the National Heart Institute by Drs. Donald S. Fredrickson, R. I. Levy and colleagues (1, 2). It has been shown that hyperlipoproteinemias are of two general classes: primary (an inherited condition, the effects of which can be adversely or beneficially influenced by diet, weight, exercise, and medication), and secondary (a condition caused by another illness such as diabetes, alcoholism, nephrosis, etc., which will subside when the primary condition is corrected).

When a hyperlipoproteinemia does exist, it may belong to any of five different syndromes—each of which requires different diet and drug therapy for successful treatment. Contrary to common belief a stringent low-fat diet is not beneficial for all types of hyperlipemia and may even be harmful in some cases. Similarly a drug which is highly effective for one type may be useless for another. If left untreated, hyperlipoproteinemia can often lead to serious or fatal illness involving the vascular system, the heart, the pancreas, liver, spleen, eyes or intestines; skin and muscle lesions, and other abnormalities.

Hyperlipemia can often be diagnosed long before the appearance of any clinical symptoms—some types in infancy or early childhood and may usually be treated successfully by diet or drug therapy. The earlier the condition is discovered, the more effective the treatment tends to be. Many apparently healthy people, destined to be future victims of heart attack, stroke and a host of lesser disorders, could be diagnosed and placed into preventive therapy. Realizing the importance of recognizing hyperlipemic types among Puerto Ricans we have been applying the system devised by Fredrickson to patients who, according to their physicians, are hyperlipemic suspects.*

The various electrophoretic patterns have been reviewed and illustrated in a previous publication (3). Type I hyperlipoproteinemia has been reviewed more recently, with clinical description of three cases, by Maldonado *et al* (4), from the University of Puerto Rico School of Medicine Hospital. Type III hyperlipoproteinemia is the most difficult to characterize from a biochemical standpoint. In this type the beta lipoproteins are abnormally laden with glyceride and can be found along with prebeta lipoprotein in the very low density lipoprotein fraction (VLDL). The lipid-burdened beta lipoprotein in this disorder is abnormal in composition and density; it usually has a "broad" or indefinite beta mobility on electrophoresis. This disorder requires the use of the ultracentrifuge for confirmation of diagnosis. After ultracentrifugation at serum density for sixteen hours, the VLDL contains abnormal beta-migrating lipoproteins (2).

Treatment of hyperlipoproteinemias has been reviewed in an excellent medical progress article by Lees *et al* (1971), (7).

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* Patients have been referred from the Veterans Hospital, University of Puerto Rico Hospital, other hospitals, as well as private physicians.

Material and Methods

Materials and methods have been published elsewhere (3). A few additional observations merit inclusion at this time. Plasma for electrophoresis of lipoproteins should be obtained from blood kept cold and collected in ethylene diaminetetraacetic acid (EDTA). The plasma may be stored for several days at 4°C but never frozen, since this irreversibly alters many lipoprotein patterns. All plasma samples for lipoproteinemic studies should be drawn after a 16 hour fast. The appearance of the serum or plasma after sitting in the refrigerator at 5°C overnight may be of help in distinguishing Type I from Type V. Type I will form two layers, a top creamy layer and a lower clear layer, while Type V will form a top creamy layer and a turbid lower layer. Further characterization, especially to distinguish Type III from Type IV is not possible by lipid analyses alone. Type III is better distinguished by the appearance of the "broad-beta" band on paper electrophoresis. Confirmation of "broad-beta disease" requires ultracentrifugal studies of sera from Type III cases (2).

Normal lipid values established for our laboratory when these studies began in 1966 are as follows: serum cholesterol, up to 250 mg percent; serum triglycerides, up to 150 mg percent; serum phospholipids, up to 250 mg percent.

Results

Results are summarized in table form (Tables I, II, III, and IV). A total of 188 cases of hyperlipoproteinemia have been classified among Puerto Ricans.

Type I: Five cases have been classified, all children, ranging from 42 days old to 14 years old. Post-heparine lipolytic activity was determined in four cases; all four had apparent deficiency of the enzyme lipoprotein lipase. Results of serum lipids are given in Table I for each case. Four of the cases are females. The only male case is the brother of case No. 2.

Type II: Eighty one cases have been classified. Average age is 47 years. Average cholesterol 328 mg percent, average triglycerides 146 mg percent, average phospholipids 331 mg percent (Table II).

Type III: Seven cases appear to have a "broad-beta" electrophoretic pattern. Results of serum lipids are given for each case in Table III. Confirmation of "broad-beta disease" is pending ultracentrifugal studies of their sera.

Type IV: Sixty six cases. Average age 46 years. Average cholesterol 262 mg percent; average triglycerides 327 mg percent; average phospholipids 327 mg percent (Table II).

Type V: Twenty nine cases. Average age 36 years. Average cholesterol 400 mg percent; average triglycerides 1,463 mg percent, average phospholipids 467 mg percent (Table II).

Review of clinical records has revealed evidence of

cardiovascular disease in 57.5 percent of Type II cases, 42 percent of Type III, 34 percent of Type IV, and 24 percent of Type V. Glucose tolerance was abnormal in 78 percent of Type II, 100 percent of Type III, 85 percent of Type IV, and 62 percent of Type V cases. Hyperuricemia was found in 80 percent of Type II, 42.5 percent of Type III, 67 percent of Type IV, and 82 percent of Type V (Table IV).

Discussion

Out of the five cases with Type I hyperlipoproteinemia reported in this paper, three have been reviewed by Maldonado *et al* (4). The only male case was the brother of case No. 2 (Table I). He was asymptomatic, but had splenomegaly, a functional heart murmur, and many foamy histiocytes in the bone marrow (4). Case No. 1 (Table I), upon review of clinical record at



Fig. 1: Case No. 4, Type I hyperlipoproteinemia, is doing well at two years of age on a low-fat formula.

TABLE I: TYPE I HYPERLIPOPROTEINEMIA

	Case No.	Age	Sex	Cholesterol (mg percent)	Triglyceride (mg percent)	Phospholipids (mg percent)
FPM	1	2 mo.	F	85	210	172
MLA	2	14 yr.	F	119	416	154
MLR	3*	11 yr.	M	133	877	195
MLL	4	42 da.	F	539	5, 179	408
SLM	5	14 mo.	F	70	200	159

* - Case No. 3 is the brother of Case No. 2

TABLE II: SUMMARY OF HYPERLIPOPROTEINEMIC TYPES II, IV, AND V

Type	No. of Cases	Age (Yrs.) Mean \pm S.E.M.*	Cholesterol (mg percent) Mean \pm S.E.M.	Triglyceride (mg percent) Mean \pm S.E.M.	Phospholipids (mg percent) Mean \pm S.E.M.
II	81	47 \pm 1.2	328 \pm 10.4	146 \pm 7.9	331 \pm 13.4
IV	66	46.0 \pm 1.1	262 \pm 8.5	327 \pm 19.2	327 \pm 10.3
V	29	36.5 \pm 2.0	400 \pm 35.4	1463 \pm 245.0	467 \pm 39.0

*S.E.M. = Standard error of the mean.

TABLE III: TYPE III HYPERLIPOPROTEINEMIA *

	Case No.	Age (Yrs.)	Cholesterol (mg percent)	Triglycerides (mg percent)	Phospholipids (mg percent)
C. P.	1	43	233	387	359
G. P.	2	33	354	631	486
L. M.	3	36	398	310	—
O. J.	4	44	306	226	276
R. I.	5	59	275	270	335
V. G.	6	45	255	202	267
V. H.	7	21	491	402	401

* Characterized by a "broad-beta band" by paper electrophoresis; pending confirmation of "broad-beta disease" by ultracentrifugal studies of serum.

TABLE IV: INCIDENCE OF CARDIOVASCULAR DISEASE (CVD), CARBOHYDRATE INTOLERANCE (Abn. G.T.T.), AND HYPERURICEMIA IN HYPERLIPOPROTEINEMIC CASES (PERCENT OF CASES CHECKED)

Type	C. V. D. (Percent)	Abn. G.T.T. (Percent)	Hyperuricemia * (Percent)
II	57.5	78	80
III	42	100	42.5
IV	34	85	67
V	24	62	82

* Hyperuricemia = serum uric acid above 6.0 mg percent.

TABLE V: AGE DISTRIBUTION OF TYPE II CASES AND EVIDENCE OF CVD, GLUCOSE INTOLERANCE, AND HYPERURICEMIA FOR EACH AGE GROUP

Age (Yrs.)	No. of Cases	C V D No. of Cases	Abn GTT No. of Cases	Hyperuricemia No. of Cases
0-9	1	0 (1) *	---	---
10-19	0	---	---	---
20-29	2	0 (2)	2 (2)	0 (2)
30-39	15	7 (15)	8 (10)	12 (14)
40-49	29	15 (29)	18 (25)	20 (24)
50-59	28	21 (28)	20 (25)	15 (19)
60-69	3	1 (2)	1 (2)	1 (2)
70-79	3	2 (3)	3 (3)	3 (3)
Total	81	46 (80)	52 (67)	51 (64)

* Figures in parenthesis represent the number of cases checked for each test and age group.

University of Puerto Rico Hospital, was found to have a final diagnosis of congenital heart disease, endocardial cushion defect, Down's syndrome, congestive heart failure, and bilateral pneumonia (April, 1971). Case No. 4 (Table I) was a problem feeder (constant vomiting), noticed to have orange blood; she had, when she was forty two days old, anemia (hematocrit 19 percent), massive hepatosplenomegaly, pulmonary edema,

duodenal ulcer, perforated, operated. She also had total body exchange transfusion. (Personal communication by referring physician). She is doing well with a low-fat milk formula (Fig. 1).

Regarding the *Type II* cases, it is of interest that the youngest case encountered is a nine year old girl referred by the University of Puerto Rico Dermatology Department. She had a cholesterol of 605 mg percent, trigly-

cerides of 89 mg percent, and phospholipids of 474 mg percent. She is the only case in the first age group with no evidence, to our knowledge, of heart disease, diabetes or hyperuricemia. She may be a case of familial Type II hypercholesterolemia. No Type II cases have been encountered between the ages ten to nineteen years old. Only two cases of Type II are between twenty and twenty nine years old. Both cases in this age group are diabetics, with no evidence of heart disease or hyperuricemia (Table V). Fifteen cases fall in the thirty to thirty nine years age bracket; seven have heart disease; eight have abnormal glucose tolerance; twelve have hyperuricemia; one has diagnosis of fatty liver, jaundice, hepatitis, and alcoholism; another is an alcoholic with hepatitis and cirrhosis of the liver (Table V). Twenty nine cases fall between forty and forty nine years old; fifteen are known to have heart disease; eighteen have abnormal glucose tolerance; twenty have hyperuricemia; two have cirrhosis of the liver; one died from heart disease (he also had diabetes and gout). Twenty eight cases belong between ages fifty to fifty nine; twenty one have evidence of heart disease; twenty have abnormal glucose tolerance; fifteen have hyperuricemia, one female case has xanthoma plana of many years duration; one has hyperthyroidism and diabetes; another has acromegaly, heart disease, diabetes, and hyperuricemia.

Three cases fall between ages sixty to sixty nine years: one died of heart disease; another has diabetes, hyperuricemia, and is the father of the second youngest Type II case (a twenty year old female with juvenile diabetes and obesity). The record of the third case is incomplete. Three cases are included between seventy and seventy nine years; one died (fasting blood glucose 258 mg percent; uric acid 9.1 mg percent, no evidence of heart disease in clinical record, blood pressure 160/70); the other two have heart disease, diabetes, and gout (Table V).

Regarding the seven cases that appear to have Type III hyperlipoproteinemia, one falls in the twenty to twenty nine years age bracket. He is a diabetic with hyperuricemia. Two cases are between thirty and thirty nine years old; one has abnormal glucose tolerance, hyperuricemia, and history of pancreatitis, the other was a thirty six year old male with history of cardiovascular disease who died with a final diagnosis of chronic glomerulonephritis; he was also intolerant to carbohydrate and had hyperuricemia. Three cases are in their forties; two have cardiovascular disease, one has a diagnosis of multiple myeloma. He also has abnormal glucose tolerance and hyperuricemia. The two other

cases are also intolerant to carbohydrates; their uric acid levels are normal. Only one case falls in the fifty to fifty nine years age bracket. He has abnormal glucose tolerance and normal uric acid (Table VI).

It is of interest that only two Type IV cases fall in the twenty to twenty nine years age bracket. There is no evidence of cardiovascular disease in these patients. The youngest case is a twenty two year old soldier admitted with malaria (*P. vivax*). He had initially triglycerides of 291 mg percent, normal G. T. T., and normal uric acid. The hypertriglyceridemia subsided with the treatment for malaria. The second patient is a twenty seven year old case with cirrhosis of the liver and diabetes (Table VII). There are ten Type IV cases between thirty and thirty nine years of age; only two show evidence of cardiovascular disease, eight have abnormal G. T. T. and four have hyperuricemia (Table VII). A thirty eight year old patient died at another hospital. His record at the VA Hospital revealed the following diagnoses: cirrhosis of the liver, hepatitis, alcoholism, drug addiction, and epilepsy. GTT and serum uric acid were both normal. Another patient, thirty nine years old, has hepatitis, diabetes, and gout. The largest group among the Type IV cases falls in the forty to forty nine years age group. There are thirty four cases in this group, out of which eleven show evidence of cardiovascular disease, twenty five have abnormal GTT, and nineteen have hyperuricemia (Table VII). The second largest age group among the Type IV cases falls between fifty to fifty nine years old. There are sixteen cases belonging to this group; ten show evidence of cardiovascular disease; twelve have abnormal glucose tolerance, and nine have hyperuricemia. A fifty one year old patient died suddenly while travelling in Spain. He had cardiovascular disease, normal glucose tolerance, and hyperuricemia. He was receiving treatment with Atromid under the supervision of a private physician; his lipids had improved, but his serum uric acid had increased during treatment. Another patient, a fifty five year old case with heart disease, has diabetes and gout, and is the father of a thirty five year old Type V case. Only three Type IV cases have been classified between sixty and sixty nine years of age. All three have abnormal glucose tolerance; one has hyperuricemia. One of the cases in this group is a sixty six year old female patient from the Dermatology Department of the University of Puerto Rico Hospital with eruptive xanthomas, having initially triglycerides of 716 mg percent, cholesterol of 444 mg percent, and phospholipids of 536 mg percent. She was treated with Atromid (personal communication

TABLE VI: AGE DISTRIBUTION OF TYPE III* CASES AND EVIDENCE OF CVD, GLUCOSE INTOLERANCE, AND HYPERURICEMIA FOR EACH AGE GROUP

Age (Yrs.)	No. of Cases	C V D No. of Cases	Abn GTT No. of Cases	Hyperuricemia No. of Cases
20-29	1	—	1 (1) **	0 (1)
30-39	2	1	2 (2)	2 (2)
40-49	3	2	3 (3)	1 (3)
50-59	1	—	1 (1)	0 (1)
Total	7	3	7 (7)	3 (7)

* Characterized by a "broad-beta" band by paper electrophoresis; pending confirmation of "broad-beta disease" by ultracentrifugal studies.

** Figures in parenthesis represent the number of cases checked for each test and age group.

TABLE VII: AGE DISTRIBUTION OF TYPE IV CASES AND EVIDENCE OF CVD, GLUCOSE TOLERANCE AND HYPERURICEMIA FOR EACH AGE GROUP

Age (Yrs.)	No. of Cases	C V D No. of Cases	Abn GTT No. of Cases	Hyperuricemia No. of Cases
20-29	2	—	1 (2) *	0 (1)
30-39	10	2	8 (9)	4 (8)
40-49	34	11	25 (30)	19 (26)
50-59	16	10	12 (14)	9 (13)
60-69	3	—	3 (3)	1 (2)
70-79	1	—	1 (1)	1 (1)
Total	66	23	50 (59)	34 (51)

* Figures in parenthesis represent the number of cases checked for each test and age group.

by referring physician); her skin lesions cleared, and her lipids improved after two months of treatment (triglycerides of 381 mg percent, cholesterol of 246 mg percent, and phospholipids of 377 mg percent). There is no evidence of cardiovascular disease in any of these three cases. There is only one Type IV case over seventy years of age. This is a seventy four year old patient hospitalized for a hernia operation. His blood pressure was reported as 134/70, weight 202 lbs., height 5'7-1/2". There is no evidence of cardio-

vascular disease in his record. He has a slightly abnormal GTT and hyperuricemia. Both parents died of heart disease at ages eighty one (his father), and seventy eight (his mother) (Table VII).

Twenty nine cases have been classified as Type V. Of these only two are between ten and nineteen years old. One is a twelve year old girl with lipoatrophic diabetes (from the Endocrinology Unit of the University Hospital), the other is a fourteen year old girl with juvenile diabetes and xanthomas, referred by the Derma-

TABLE VIII: AGE DISTRIBUTION OF TYPE V CASES AND EVIDENCE OF CVD, GLUCOSE INTOLERANCE AND HYPERURICEMIA FOR EACH AGE GROUP

Age (Yrs.)	No. of Cases	C V D No. of Cases	Abn GTT No. of Cases	Hyperuricemia No. of Cases
10-19	2	—	2 (2) *	—
20-29	3	—	2 (3)	1 (1)
30-39	12	2	5 (10)	10 (12)
40-49	11	4	7 (11)	7 (9)
50-59	1	1	1 (1)	1 (1)
Total	29	7	17 (27)	19 (23)

* Figures in parenthesis represent the number of cases checked for each test and age group.

tology Department of the University Hospital (Table VIII). Three cases fall in the Type V class belonging to the twenty to twenty nine years age bracket. Two are diabetics, one has hyperuricemia. Twelve Type V cases fall in the thirty to thirty nine years age group. Of these, two have evidence of cardiovascular disease, five have abnormal glucose tolerance (Table VIII), and ten have hyperuricemia. One is a thirty five year old case with liver cirrhosis due to alcoholism. Another was a thirty nine year old case with history of cardiovascular disease who died. He had a final diagnosis of chronic glomerulonephritis. There are eleven Type V cases in the forty to forty nine years age group. Four have evidence of cardiovascular disease, seven have abnormal glucose tolerance, and seven have hyperuricemia. One is the forty year old father of one of the cases in the twenty to twenty nine years age bracket. Another case, who is forty five years old, has heart disease, diabetes, and liver cirrhosis. There is a forty six year old case with a diagnosis of eruptive xanthomas; he is also diabetic and has high blood pressure. In the fifty to fifty nine years age group only one case has been classified as Type V. He has cardiovascular disease, diabetes, and hyperuricemia (Table VIII).

Once the type of hyperlipoproteinemia is recognized it is possible to select the appropriate dietary or drug regime that may be most beneficial in bringing back to normal the serum lipid levels (5, 6, 7).

Type I is fat induced and improves on a low-fat diet. It may also improve with medium-chain triglycerides, which do not form chylomicrons. Type II can improve

with a low-cholesterol diet, lowering ingestion of saturated, and increasing ingestion of polyunsaturated fats. In the familial Type II adult, diet alone may not be sufficient in controlling the hyperlipemia, making it necessary to use hypolipemic drugs, such as cholestyramine. In the non-familial Type II, diet alone may control the hyperlipemia. Type III, better known as "broad-beta disease", a rare condition which has been characterized recently as a new syndrome with an abnormal type of beta-lipoprotein, may be controlled by weight reduction to ideal body weight; followed by a maintenance diet balanced in fat and carbohydrate (40 percent of calories from each), and low in cholesterol. Diet alone may be sufficient in bringing back to normal the serum lipids. Clofibrate (Atromid-S®), has been used with some success in Type III. Type IV is associated with coronary disease in young adults and with diabetes. It may be controlled by weight reduction to ideal body weight followed by a diet low in carbohydrates and alcohol, since a dietary excess in either of these will tend to increase the levels of triglycerides of endogenous nature. Type V is associated with abnormal lipid and carbohydrate metabolism, being inducible by both carbohydrate and fat. Patients seem to improve by reduction to ideal body weight, followed by a maintenance diet low in carbohydrate, moderate in fat and consequently, very high in protein. This diet is very difficult to follow for an indefinite period of time without constant encouragement from the physician and dietitian. It remains for the future the development of a drug that may be useful in controlling hyperlipemia of Type V.

Summary

A progress report is presented of hyperlipoproteinemic types among Puerto Ricans. A total of 188 cases have been classified according to the system of Fredrickson. The largest groups are Types II and IV, followed by Type V. Seven cases appear to belong to Type III by paper electrophoresis of lipoproteins. Only five cases, all children, have been classified as Type I. Results are presented to indicate, for each group: age, serum cholesterol, serum triglycerides, serum phospholipids, as well as the incidence of cardiovascular disease, abnormal glucose tolerance, and hyperuricemia. Age distribution for each group is also presented (by decades) to include: number of cases, incidence of cardiovascular disease, abnormal glucose tolerance, and hyperuricemia.

Resumen

Se informa el progreso del estudio de tipos hiperlipoproteinémicos entre puertorriqueños. Un total de 188 casos han sido clasificados de acuerdo al sistema de Fredrickson. El mayor número de casos pertenece al Tipo II, siguiéndoles en frecuencia los del Tipo IV y luego los del Tipo V. Siete casos aparentemente pertenecen al Tipo III, de acuerdo a la electroforesis de papel de lipoproteína. Solamente cinco casos han sido clasificados como Tipo I, todos menores de 15 años de edad. Se presentan los resultados para cada grupo incluyendo edad, niveles de colesterol, triglicéridos y fosfolípidos séricos. También se incluyen datos sobre la incidencia de enfermedad cardiovascular, tolerancia de glucosa anormal e hiperuricemia. También se presentan para

cada grupo la distribución por edades (en décadas) del número de casos, incidencia de enfermedad cardiovascular, tolerancia de glucosa anormal e hiperuricemia.

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PREVENTION OF COMPLICATING EMOTIONAL PROBLEMS OF THE PARAPLEGIC

Herman J. Flax, MD, FACP

The over-all program of paraplegic rehabilitation begins with this premise: Although paralyzed below the waist, the paraplegic has two good upper extremities, made even stronger and more perfect through training in crutch walking and arts and crafts. These arms can produce just as much as those of any "normal" individual in appropriate employment. The difference lies only in the mental capacity of the paraplegic and how far the physical trauma and resulting complications have affected this thinking. It is much easier to rehabilitate a paraplegic physically than mentally. But, even this is not too difficult if the patient is treated in the proper environment from the very beginning of his rehabilitation program. It is only with adequate and complete training that the paraplegic can be restored successfully to his community.

Very few of our hospitals are properly equipped to treat paraplegics adequately. Freeman (1) has outlined this therapy in his well-documented paper. He states, "The essentials of hospital care of the paraplegic patient is a combined program, consisting of: Proper nursing care, proper care of bowel and bladder, proper care of skin and constant medical supervision to prevent and treat all complications. Of equal importance is the necessity to constantly be on the alert for complicating emotional reactions and help the patient to accept the reality of his difficulty."

Understanding and planning a program to avoid this problem is the topic of our discussion today.

A study (2) made at the Bronx VA Hospital sheds a great deal of light on the basic anxieties of the paraplegic. To paraphrase this study, the following question was asked a group of graduate students in physical education at a round table discussion on understanding the emotional problems of the paraplegic, "If you were a paraplegic with loss of bowel and bladder control, paralysis of the lower extremities and inability to

have sexual intercourse, in what order would you desire return of the above functions provided this were possible?" Every single one of the group voted for return of sexual powers first, and then the majority preferred recovery of the use of their lower extremities and, lastly, bowel and bladder control.

Not so, the paraplegic veterans! They all wished for bowel and bladder control first, then power to ambulate and ability to copulate lastly. Quite a difference of opinion! But think of the importance of bowel and bladder control in all of our daily activities, and then the reason why the paraplegic veterans picked this as the most necessary factor in their program can be understood. Many, but many times, paraplegic patients have said to me, last night I had such a wonderful time at the party, the show, or the ballgame, until I soiled my pants. This abruptly terminated the evening for them.

The paraplegic like all humans, tends to maintain his existence under optimum conditions with the minimal expenditure of energy. The paraplegic, who does not want to learn crutch walking or who does not continue crutch walking at home is not lazy. He is simply taking the path of least resistance. Certainly, it is easier to ride than to walk! But, even those who are poorly motivated psychologically must be made to understand the importance of the upright position to prevent the formation of renal calculi, the number-one killer of paraplegics.

Dr. A. D. Mueller (3), Chief Clinical Psychologist, Kennedy VA Hospital, is also of this opinion. It is interesting to review his discussion of this problem. He states: "In a study of personality problems of patients with spinal-cord injuries, we found the main problem in rehabilitation was overcoming the resistance found in many patients to activities requiring physical and mental effort on their part. Some characteristic reactions of patients were: (1) indifference, ambivalent or depressive attitudes toward the future and the possibility it could hold for them socially and vocationally; (2) indecisiveness and feelings of insecurity; and, (3) assuming a submissive and de-

pendent role in life with accompanying immature emotional behavior. The problem in my opinion, is essentially one of values and motives. Does the patient think enough of his crutch walking to give him a feeling of independence and security, or does he gain greater emotional satisfaction by assuming a submissive and dependent role in life? Choice between crutch walking or of being satisfied with a wheel-chair existence will depend on which of the two attitudes predominantly prevails in the patient."

The methods of achieving a "total-push" program for emotional rehabilitation of the paraplegic involves psychotherapy every minute of the day by every single person coming in contact with the patient from the ward boy, who makes the bed, to the therapists, who rehabilitate the patient vocationally and physically. Sympathetic understanding, yet firm conviction, is in order to stimulate the patient continuously to greater effort.

A successful rehabilitation program is one that never leaves the patient alone for a single moment in the day. The daily program must be arranged in hourly classes, just as in public schools, and the schedule written out on a card and given to the patient, so that he will know his daily log. In this way, every hour will be occupied. The patient will have little time to think about himself, and when the end of the day comes, he will fall into bed exhausted and sleep soundly until the next morning.

The paraplegic, as he begins to show less interest in an activity, must be encouraged and even firmly directed to develop new fields of endeavor, new avenues of satisfaction, new lines of thoughts. These hobbies, many of them of a pre-vocational nature, may turn out to be the very stimulus necessary to snap the patient out of his emotional slump. In this respect, the occupational, manual arts and the educational therapists are excellent psychologists and really lay the foundation for the patient's future.

Included in this daily schedule must be a time for the paraplegic to "blow off steam" or more scientifically stated, the release of inner tensions. A period must be set aside for the patients to get together in small groups with their physician and talk about themselves. This is known as "group therapy", a nondirective procedure of psychotherapy. This method has proved to be very successful at the Bronx VA Hospital and has been reported by Dr. Robert S. Morrow (4). His conclusions agree with earlier investigators that these patients gain a better insight and understanding into their difficulties, and the beginning predominance of negative self-references gives way in short time to increased positive references. The-

re is a shift from self-depreciation to self-approval; an improvement in adjustment as the attitude towards self changed. Most significantly is the fact that the individuals acceptance of himself is related to the degree to which he accepted others.

As the paraplegic becomes more and more independent, his program must include more and more time for fraternizing with the outside world. This is the real advantage of the automobile which is given the patient by the Veterans Administration. It should not be thought of as a reward for his battle wounds as, unfortunately, do many of the paraplegics.

This brings to mind a little story of one of my paraplegic patients at San Juan VA Hospital. This man was a taxi-cab driver before the war. So, when the discussion came up concerning vocational rehabilitation, I mentioned casually that he had no problem. With his new automobile he could return to his former employment of driving a taxi-cab. The patient became exceedingly angry and blurted out that the car was given for pleasure and not for work. He signed out of the hospital the next day, even leaving his braces behind, and still refuses to continue his rehabilitation program. From our social service follow-up I understand that this patient moved into a suitable home but sits all day long in his wheel chair. He is a frequent patient of the GU ward at the VA Hospital. Unless he gets up on his feet with his braces, his days on this earth are numbered.

What is as important as the physical and vocational rehabilitation of the patient is the need to educate the public to accept the paraplegic (and all other seriously handicapped individuals) as human beings and not as freaks of nature. This thought is constantly in the minds of these patients, and this fear of the future in society is a great detriment to their motivation for rehabilitation. The war casualties and the civilian crippled and disabled cannot be shut up forever in the confines of hospitals and nursing homes if we abide by our present definition of rehabilitation. The fact remains, a paraplegic has a good mind and two perfect upper extremities, and he must be counted along with all the general public in the conservation as well as maximum use of our existing manpower.

This point bears emphasizing. It is extremely important that the paraplegic patients get out into society and learn how to face the world once again. Society must accept them not as disabled individuals but must be made to understand that the paraplegic is as capable of producing as much as the "normal" citizens of any community in the proper job.

To help them get established in their communities, the Federal Government provides special homes for service-connected paraplegic veterans. True, these are wheelchair houses with special facilities for their comfort. But all of us prepare our homes to satisfy our own needs. Therefore, we, so-called able-bodied citizens, must not look upon these dwellings as special decorations in our communities but must accept them and their occupants as we would any neighbor (5). This will go a long way towards cancelling the paraplegic's fear of the future, of not being accepted by society once he has left the sheltered confines of the hospital.

Finally, there is a great need for a follow-up service for the paraplegic patient. It is not enough to orientate him into society by interviewing him and his family in the hospital. There is still the urgency to evaluate his progress in the environment of his home and community. Rehabilitation means retraining the disabled individual to live and work with what is left, not only in the sheltered environment of a rehabilitation center but also in his own home.

We must make sure that the patient uses his training in the community, otherwise his program of rehabilitation is not complete. Therefore, the social worker and even the vocational counsellor must visit the home and community of the patient and become familiar with the family, neighbors and vocational opportunities available to the paraplegic. This is especially important in the towns and rural districts of Puerto Rico.

"Life for all of us is a cooperative enterprise: our success in this enterprise depends on what we as individuals and what our social group put into it. For the disabled this equation for living is the same. Success still depends on what the individual and his community put into the project. The only difference is one of degree, for both the disabled and his community must put more into the enterprise to help meet — to help compensate — the deficits of disability" (6).

This cooperation should include all the groups interested in rehabilitation in the community: private, city, insular and federal. As yet, little has been done in Puerto Rico to sow the seeds of understanding and cooperation amongst these agencies.

Suffice it to say, there is no clinic able to meet the rehabilitation needs of paraplegics or the severely disabled in Puerto Rico. Yet, there are many agencies capable of organizing this Paraplegic Rehabilitation Center. How much more important to the Island of Puerto Rico would it be to combine the resources of

all our agencies and organize this center once and for all instead of spending great sums of money sending a few to the States for expert care or paying for inadequate nursing care in local hospitals.

This is not a difficult plan. Only, it requires the devotion of a few social-minded individuals who understand that the foundations of rehabilitation lie with the community as a whole. The failure of the community to do its part has been the chief factor in the failure to rehabilitate paraplegics in Puerto Rico.

In summary, let me briefly review the facts presented in this discussion. First, life must be saved, and all our efforts must be directed towards this end. Then, a full program of physical activity must be devised in order to prevent the patient's killing himself with renal failure, the result of kidney-stone formation from inactivity. His daily program in the hospital must be a rigid one with every hour taken up with physical, educational and vocational rehabilitation, a "total push" rehabilitation program. Time must be left for group psychotherapy, when the patient can discuss his emotional problems. Finally, he must become a part of the community, and for this not only the patient but society must be trained to accept him. Lastly, a follow-up service must be developed to strengthen the social supports of rehabilitation.

A plea was made to establish a model Paraplegic Rehabilitation Center in Puerto Rico for treatment of all paraplegics as well as training of personnel.

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Editorial

En una reunión reciente de la Junta Editora del Boletín consideramos un artículo para publicación, que, a pesar de ser la condición reseñada allí una diagnosticada casi exclusivamente por medios radiológicos, en la lista de autores los radiólogos brillaban por su obvia ausencia. Mi primera reacción fue de molestia por considerarr ésto evidencia de piratería hacia mi especialidad y poca cortesía de mis colegas clínicos al no incluir algún radiólogo en la lista de créditos.

Pero al pensar detenidamente sobre el asunto luego, en mi propia intimidad, concluí que la culpa real — el peso de la responsabilidad de esta situación — no es de los clínicos que usan el material radiológico, y sí de la clase radióloga misma.

¿Por qué?

Al igual que en el resto del mundo, en Puerto Rico la necesidad de radiólogos sobrepasa tremendamente el número de ellos disponible. Y con un solo programa de entrenamiento en la especialidad existente al momento, se forman entre tres y cuatro nuevos radiólogos anualmente, un número muy inferior al necesitado. La demanda es tan grande en el área metropolitana que casi todos los residentes que terminan se quedan aquí. Son muy pocos los establecidos en pueblos de la Isla. Otro resultado de esta situación, es la abrumadora cantidad de trabajo, mayor de la que pueda manejarse por el radiólogo. Y siguiendo los dictados de la ley de oferta y demanda, dirigen éstos sus pasos al área del mejor postor: en este caso resulta ser la práctica privada de la especialidad.

Se produce entonces una escasez de radiólogos en el campo académico que asume el cariz de crisis. Al mismo tiempo afecta de tal manera la imagen del radiólogo entre sus discípulos jóvenes en entrenamiento, a tal extremo, que la orientación de la radiología actual es decisivamente alejada del campo académico y hacia la práctica privada. Pertenecer a la Facultad de Radiología de la Escuela de Medicina ya no representa un prestigio y sí un aguante mejor que el del radiólogo promedio. Aquellos de nosotros que intentamos hacer alguna labor académica la llevamos a cabo mal hecha, a medias, afectados siempre por la desagradable disyuntiva de qué nos interesa en la medicina y qué nos interesa fuera de ella. Por lo primero nos quedamos en el campo académico y pagamos el precio que económicamente significa. Por lo segundo, nos vamos a la práctica privada, y a la larga resultamos con tantos compromisos en diferentes sitios, que es broma de rigor en muchos de los hospitales más pequeños tratar de sorprender al radiólogo cuando está allí.

Como resultado directo de esta situación, la orientación fuera de academia y la enorme demanda por servicios, los radiólogos, o no tenemos la inclinación, o no tenemos el tiempo para publicar. Y la situación es doblemente triste si se considera que ante nuestra vista (literalmente) desfila lo mejor en patología que cada especialidad puede ofrecer. La inercia literaria nos afecta tan severamente que ni siquiera somos capaces de contribuir con lo poco que nos piden nuestros colegas para completar algún artículo. Por eso surgen las situaciones como la que apunté al principio de este artículo.

¿La solución?

Una perogrullada. Como diría un filósofo nativo — es cuestión de la grasa que afloja cualquier tuerca — DINERO. Salarios suficientemente atractivos para evitar que sea necesario buscar fuera del campo académico un nivel de vida sin angustias o envidia al compañero más próspero fuera. Y obviamente ésto no se conseguirá a través de subsidio directo del gobierno — no creo que po-

damos darnos ese lujo en un futuro cercano. Creo que será necesario, a través de las Leyes existentes, y de legislación nueva, ofrecer la oportunidad de que aquellos que optan por el campo académico lo puedan hacer sin grandes preocupaciones. Solamente en un clima como ese es posible crear y poner impreso el producto de la experiencia médica.

Emilio Torres Reyes, MD

FE DE ERRATA

Por la presente corregimos error en el artículo sobre marcapasos que se publicó en el Boletín de la Asociación en la edición fechada en febrero de 1972, Vol. 64, Núm. 2.

La Fe de Errata es la siguiente: Las personas que colaboraron con la Dra. Mercedes Vega Vidal en la labor secretarial fueron las Srtas. Jenny Parra y Milagros Hernández, y no las personas que aparecen mencionadas.

NOTICIAS

The American Academy of Pediatrics issues warning on use of drugs to promote weight gain:

EVANSTON, ILL. — The use of drugs to promote weight gain in children should be reserved for those children with serious nervous conditions causing loss of appetite and emaciation. Such drugs should be coupled with definite therapy aimed at the underlying problem.

This warning was sounded by the Committee on Drugs of the American Academy of Pediatrics in a statement appearing in the AAP's current Newsletter.

"It is easy to prescribe drugs for patients asking for simple answers for complicated questions," the Committee on Drugs pointed out in its statement. "However, a parent's anxiety is not an indication for the use of drugs to promote weight gain in a normal child."

In its statement, the Committee called attention to the drug cyproheptadine, an antihistamine and serotonin inhibitor which has proven effective in promoting weight gains in numerous studies.

"Although the precise mechanism of production of weight gain is unknown, it can be speculated that cyproheptadine acts as an appetite stimulant through central nervous system serotonin inhibition," the statement emphasized. "Balance data show increased urinary creatinine and sodium, which is attributed to increased food intake."

The Committee on Drugs went on to state that cyproheptadine causes frequent side effects including drowsiness which might impair school performance.

Other side effects include dizziness, dry mouth, anxiety, and skin rash.

"There seems to be a strong drive in human beings to want to resemble each other in body build," the Academy emphasized. "The parent of the short and/or thin child wants the child to look more 'normal,' and when the child is old enough to resent being called 'shorty' or 'skinny,' he will want to look like his taller, mesomorphic (muscular) peers."

The statement further indicated that pediatricians usually respond to parents' requests for an appetite stimulating medication by reassuring them that there is nothing wrong with being thin, in contrast with the medical problems associated with being overweight.

We quote below correspondence received from the American Medical Association. We encourage physicians to respond promptly and completely to this survey, because its success depends upon the response of the members:

Dear AMA Member:

The House of Delegates instructed the Speaker to appoint an ad hoc Committee of the House to develop and implement a membership opinion poll on critical basic issues affecting the practice of medicine.

Attached is the first questionnaire developed by the Committee which we are asking you to *please complete and return as soon as possible*. This is an unprecedented opportunity for you, as a member of the AMA, to voice opinions which will be used in guiding the House of Delegates and the Board of Trustees in formulating policies and programs which the majority of members support.

Only summary data will be used in analyses and reports, and the anonymity of individual responses is absolutely assured.

The success of this first of a series of membership opinion polls which the Committee is planning to conduct depends upon your response.

Your cooperation is appreciated.

Sincerely,

Russell B. Roth, MD

Speaker, House of Delegates

The AMA House of Delegates at the 1971 Annual Convention took actions which would provide the AMA membership with opportunities to express their opinions on critical issues affecting the practice of medicine. A synopsis of these actions are:

Resolution 92 (A-71)

RESOLVED, That the AMA make a definite effort to determine the opinions and desires of the total membership on critical basic issues by an informed opinion poll to the entire membership; and be it further

RESOLVED, That the Speaker appoint an ad hoc committee to develop the implementation of such opinion polls.

Resolution 17 (C-71)

RESOLVED, That the AMA increase its effort through the *American Medical News* or by any other means to more frequently obtain opinions from the members of the AMA on key national issues.

Complying with these actions, the Speaker of the House appointed the following members of the House to serve on this ad hoc committee:

Henry I. Fineberg, MD, New York
H. Russell Fisher, MD, California
Richard E. Flood, MD, West Virginia
Theodore Grevas, MD, Illinois
James H. Sammons, MD, Texas, Chairman

This is the first of a series of membership opinion polls which the Committee is planning to conduct. In addition to direct mail questionnaires, the Committee also plans to use the *AM News* and *JAMA*.

TELL US WHAT YOU THINK!

HELP US FORMULATE POLICIES THAT YOU BELIEVE
ARE IN THE BEST INTERESTS OF THE MEDICAL PRO-
FESSION AND OUR PATIENTS!

OTROS COMENTARIOS

MEDICINE BY FIAT

"It was a pleasant grassy plot deep in the woods beside a rippling stream. The water came down from a mountain that could be seen towering over the trees. Below, the stream fell over a rocky cliff. The roar of the waterfall was softly evident.

"The little family had just completed a picnic and the gentle young mother had mixed water heated over a fire with clear water to give her baby a bath. Finally clean, she washed off the last residue of soap suds from his tiny form and then picked up the basin and with one quick sweep tossed its contents into the rapidly moving water. She scarcely had time for a scream before the baby disappeared over the waterfall."

This gruesome little story, the reader is assured, is based on no element of truth whatsoever. The allegory, however, is very applicable to medicine in America today. Although examples are manifold, the one in point has to do with government restrictions on hexachlorophene. A story about a baby is especially appropriate in this case as many babies may be doomed

to float over the falls if the present course is continued.

Perhaps some of the bureaucrats responsible for the latest edicts do not remember the actual fright that was felt by almost all members of the health team in any discussion of hospital based infections. It seems like yesterday that practically every medical journal had at least one article on the control of hospital infections and staph epidemics. Today these articles are very rare. It is a long time since the horror of a nursery epidemic has occurred.

Many steps were made in those days to cut down on hospital based infections. Each institution had its own infection control committee which did yeoman work. It is a fact, however, that the committees only directed the battle. The one factor which was used in practically every hospital to combat this dreadful scourge was the use of anti-infective agents. In most cases this was hexachlorophene. Practically every nursery in the country has been scrubbing every newborn with a hexachlorophene-laden detergent for the last fifteen years. In that time newborn enteritis and pyoderma has practically disappeared.

Because some monkeys get dizzy from exposure to large quantities of this substance, we are still not justified in turning one nursery into a place of death as so many were about fifteen years ago. The wash water has been tossed away and we are watching the baby go with it. How long before the pronouncements of the FDA will have reduced once great American medicine to the level of tribal witchcraft?

George A. Rowland, MD
Millville

(Permission to reprint granted by *Pennsylvania Medicine's March Issue*)

- A N U N C I O S -

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Valium® (diazepam)

For the tense cardiac patient who must be kept calm

Before prescribing, please consult complete product information, a summary of which follows:

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures.

Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision.

Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolate reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg *b.i.d.* to *q.i.d.*; alcoholism, 10 mg *t.i.d.* or *q.i.d.* in first 24 hours, then 5 mg *t.i.d.* or *q.i.d.* as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg *t.i.d.* or *q.i.d.*; adjunctively in convulsive disorders, 2 to 10 mg *b.i.d.* to *q.i.d.* **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg *t.i.d.* or *q.i.d.* initially, increasing as needed and tolerated (not for use under 6 months).

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BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

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II. Aspectos hemodinámicos y radiológicos 126

*Jorge O. Just Viera, MD, Ernesto Rivé Mora, MD, Pablo Iván Altieri, MD, Carlos Girod, MD, Olga L. Rodríguez, MD, Jorge Haddock, MD,
Carlos Méndez-Bryan, MD y Waldo López, MD*

COMPARISON OF TWO VECTORCARDIOGRAPHIC LEADSYSTEMS (BURGER AND FRANK) 133

Pieter Van Loon, MD, Amalia Martínez Picó, MD, Agustín Muñoz Santiago, MD, Charles D. Johnson, MD and Carlos Girod, MD

CONCEPTOS ACTUALES SOBRE LA ENDOCARDITIS INFECCIOSA 141

Jorge Sánchez, MD, Felipe Vizcarrondo, MD, Enrique Márquez, MD y Amalia Martínez Picó, MD

CARDIOPATIA CONGENITA SEVERA DEL RECIEN NACIDO 147

Jorge Sánchez, MD, Georgina Marroig, MD, Ofelia Rojas, MD y Amalia Martínez Picó, MD

RELACIONES ANATOMICAS ENTRE LA VALVULA PULMONAR Y LA BASE DE LA OREJUELA DERECHA 157

Renán A. Dieppa y Jorge O. Just Viera, MD

EDITORIALES 159

Hexaclorofeno

Obsolete Excuses or Obsolete Facilities?

NOTICIAS 162



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



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Before prescribing, please consult complete product information, a summary of which follows:

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Dosage: Individualize for maximum beneficial effect.

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Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

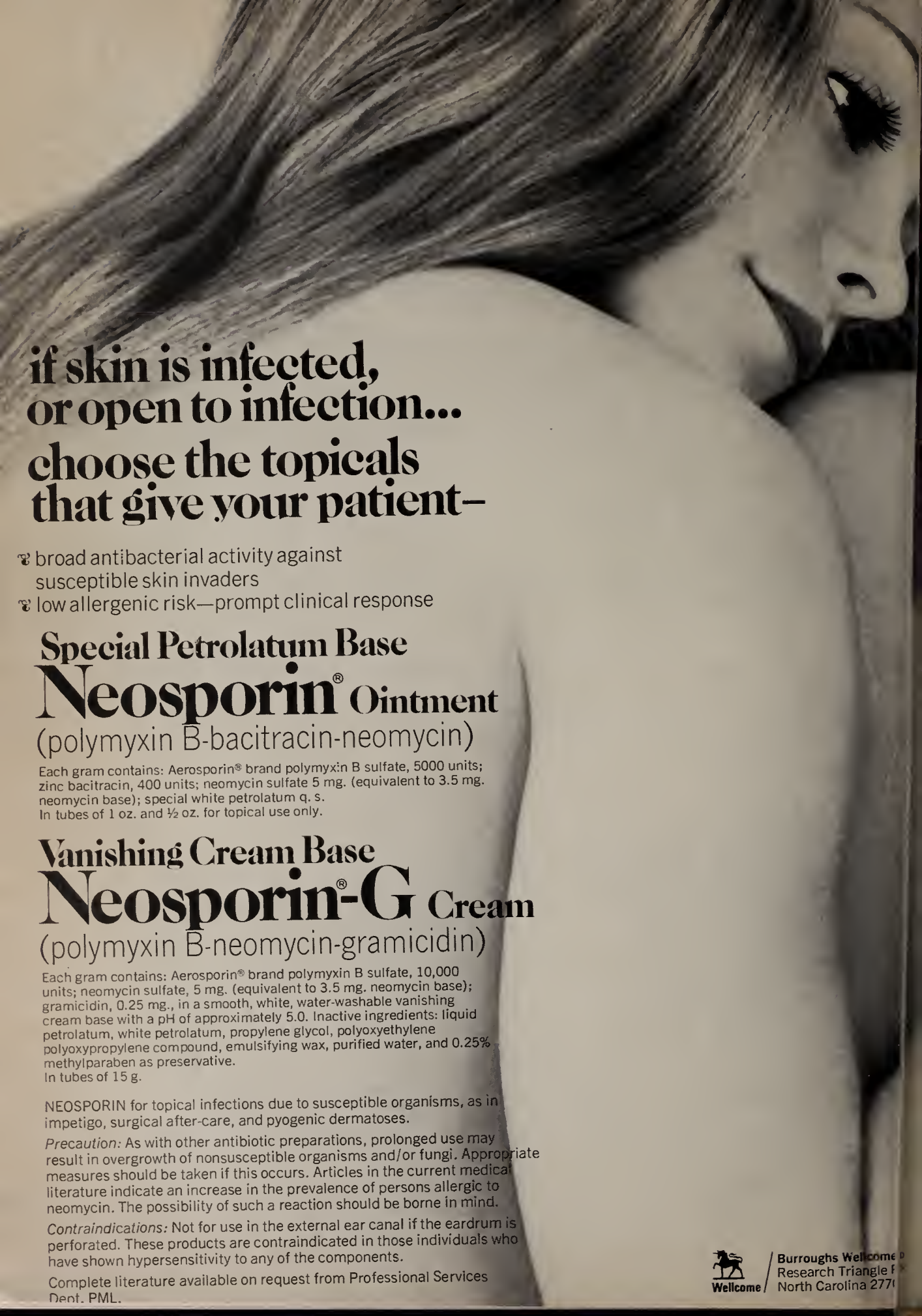
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.

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For complete details, including dosage, please see full prescribing information.

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Neosporin[®]-G Cream
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NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome
Research Triangle Park
North Carolina 27709



rheumatoid arthritic blowup ...

Tandearil® Geigy

oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

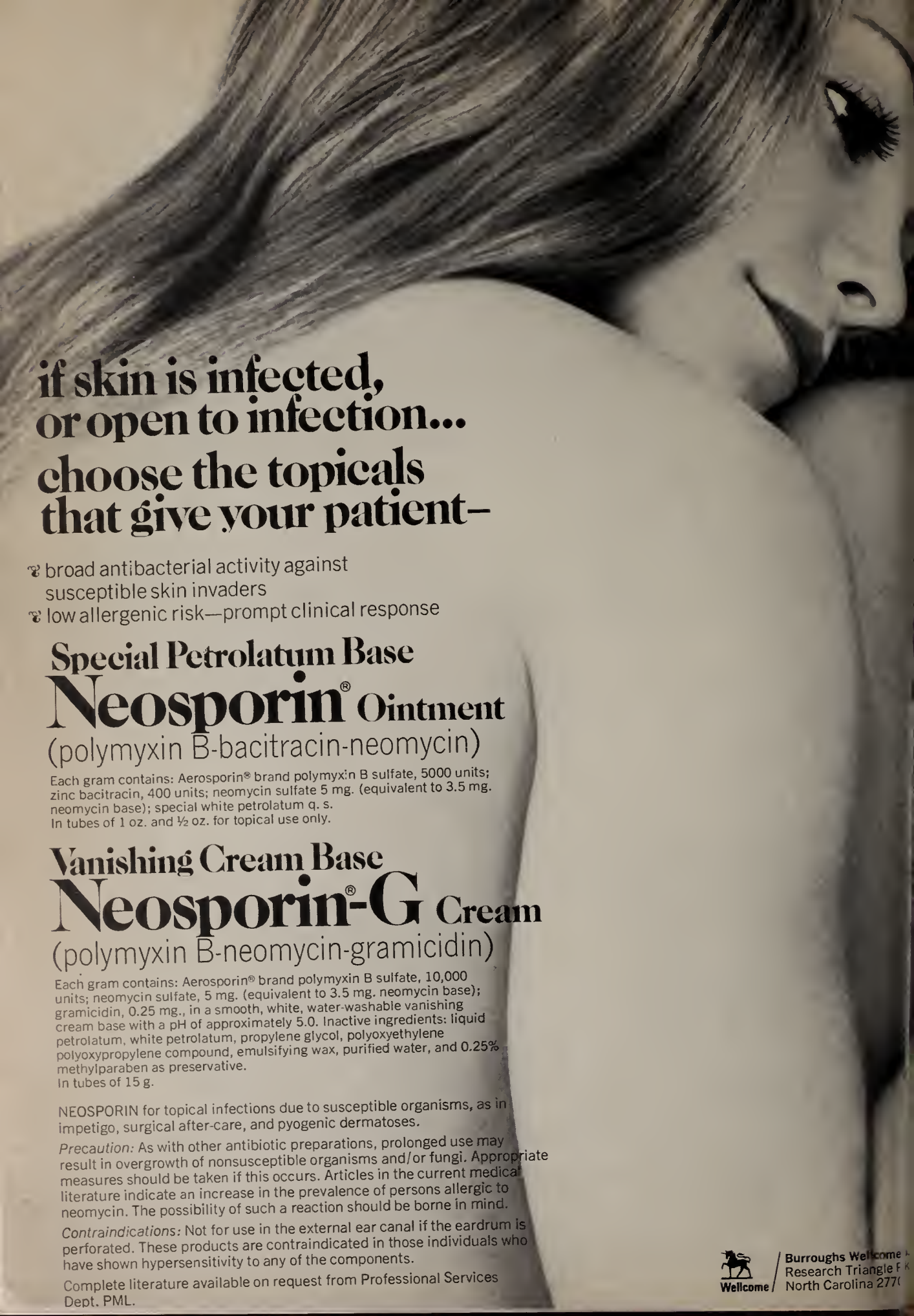
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B) 98-146-800-E

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502



**if skin is infected,
or open to infection...
choose the topicals
that give your patient—**

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin[®] Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin[®] brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
Neosporin[®]-G Cream
(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin[®] brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

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Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome
Research Triangle Park
North Carolina 27709

We're not against all her E. coli...

only the E. coli in her
urinary tract

Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. And it does not suppress normal bac-

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

Macrochantin® Capsules

(nitrofurantoin macrocrystals)

50mg./100mg.

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible on in vitro susceptibility testing. Also for treatment of urinary infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one year of age and in pregnant patients at term. The drug should not be administered to persons who have a known hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia in the primaquine sensitivity type, apparently linked to glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterranean

and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg.

EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04).



Originators and Developers of The Nitrofurans
EATON LABORATORIES
Norwich International
410 Park Avenue, New York, N.Y. 10022

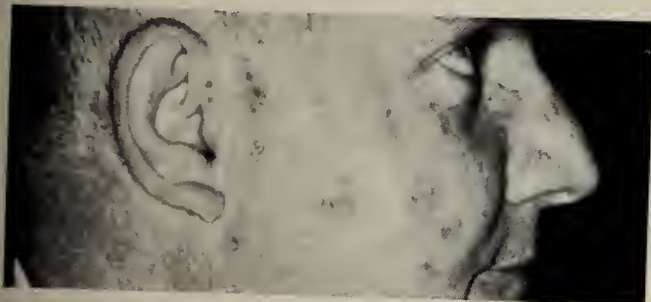
**What's
on your
patient's
face...**

**may be more important than
his chief complaint**

The lesions on his face may be solar/actinic — so-called “senile” keratoses...and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics: the typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent, and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.



Patient P.T. seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electro-surgical procedures.*

Sequence of therapy/ selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; the reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.



Patient P.T. seen on 6/12/67, seven weeks after discontinuation of 5%-FU cream. Reaction has subsided. Residual scarring not seen except for that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local — pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported — insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with non-metal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers — containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes — containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

**This patient's lesions
were resolved with**

Efudex[®] **(fluorouracil)**

**5% cream/solution
...a Roche exclusive**



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

Prompt relief of pain is a lot of what the practice of medicine is all about...East or West.

In much of the Far East, the analgesic efficacy of Empirin® Compound with Codeine would probably be measured against acupuncture, an ancient and traditional therapeutic system.

In America, codeine sets such a high standard for oral analgesia, that it has become a criterion in terms of which other major oral analgesics are most often measured.

Synthetic and other oral analgesics may offer some of the properties of codeine, but not one can provide both its benefits and potency. And codeine provides an antitussive bonus.

Empirin Compound with Codeine

is the most widely used, and probably the most pharmaceutically elegant analgesic preparation providing codeine. It's the time-tested combination for predictable pain relief... whether the pain is visceral or musculoskeletal; acute or chronic.



III New prescription flexibility. At your discretion, and where state law permits, a prescription for Empirin Compound with Codeine may now be refilled up to five times in six months.

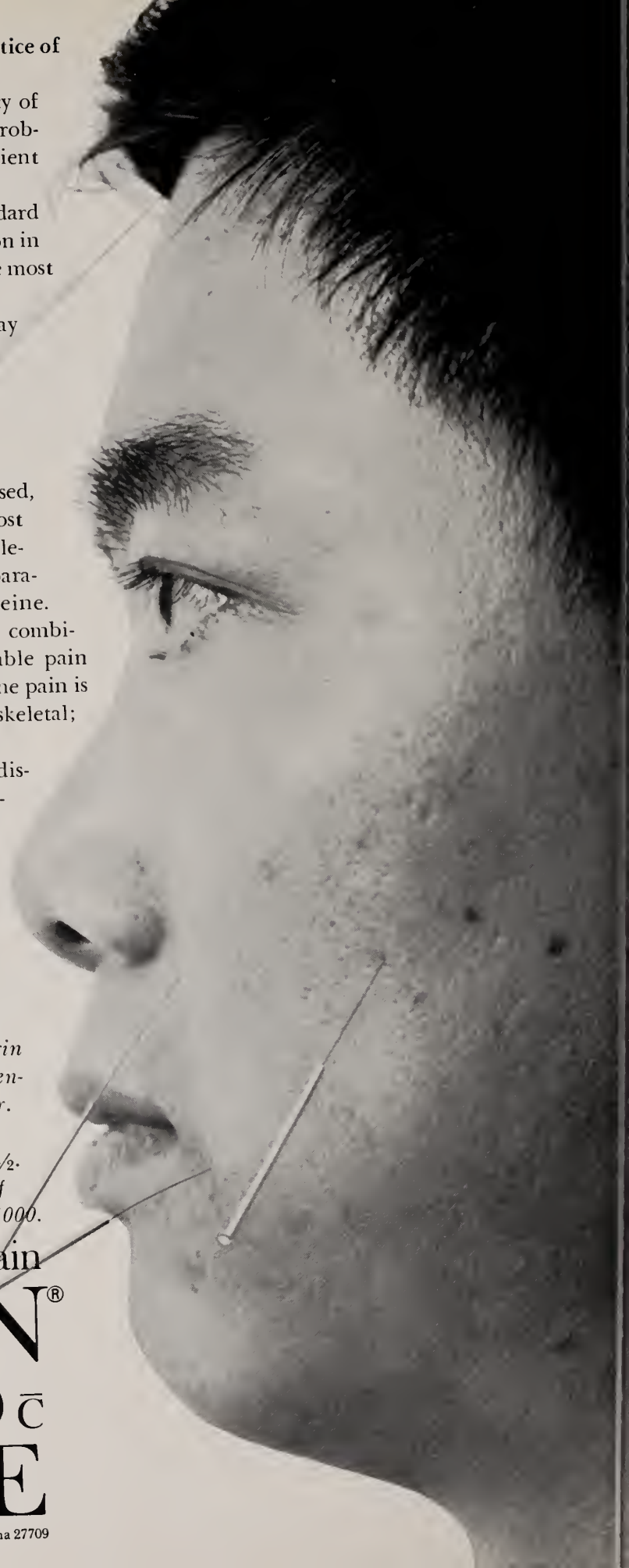
Empirin Compound with Codeine No. 3 contains codeine phosphate (32.4 mg.) gr. 1/2. No. 4 contains codeine phosphate* (64.8 mg.) gr. 1. *(Warning—may be habit-forming.) Each tablet also contains: aspirin gr. 3 1/2, phenacetin gr. 2 1/2, caffeine gr. 1/2. Bottles of 100 and 1000.*



But for relief of Western pain

EMPIRIN® COMPOUND \bar{c} CODEINE

Burroughs Wellcome Co., Research Triangle Park, North Carolina 27709



NUEVA OPERACION PARA ATRESIA TRICUSPIDEA, PULMONAR Y CONDICIONES ASOCIADAS CON MALFORMACION DEL VENTRICULO DERECHO

II. Aspectos hemodinámicos y radiológicos

Jorge O. Just Viera, MD
Ernesto Rivé Mora, MD
Pablo Iván Altieri, MD
Carlos Girod, MD
Olga L. Rodríguez, MD
Jorge Haddock, MD
Carlos Méndez-Bryan, MD
Waldo López, MD

En un informe anterior (1) se discutieron los aspectos quirúrgicos del puente atriopulmonar con homoinjerto de arteria y válvula pulmonar que proponemos para el tratamiento de atresia de la válvula tricúspide, atresia de la válvula pulmonar, hipoplasia del ventrículo derecho y condiciones asociadas, tales como ventrículo único.

Es nuestro propósito presentar los resultados de estudios hemodinámicos y exámenes radiológicos obtenidos en animales que sobrevivieron la operación por largo plazo.

Método

Cuatro perros sobrevivieron, y fueron sometidos a sondeo cardíaco bajo anestesia de barbitúricos, 4 meses, 7 meses y 10 meses (2 animales) después de la operación. El cateterismo completo derecho e izquierdo permitió la determinación del gasto cardíaco, de la resistencia vascular sistémica y pulmonar, además de las presiones en las cámaras cardíacas (Fig. 1).

Estos cuatro sobrevivientes a largo plazo, y otros animales que vivieron menos tiempo, fueron objeto de estudios radiológicos seriados por medio de angiocardiogramas. Después de intubar la vena jugular, o subsiguiente a cateterismo cardíaco, se inyectaron 20 mls. de Conray. El seriógrafo procesó dos placas por segundo por 4 segundos y una por segundo por 4 segundos adicionales. Los angiocardiogramas en algunos animales examinaron el puente atriopulmonar con injerto establecido al mismo tiempo que se obtuvo el cierre de la válvula tricúspide. Otros fueron operados en dos etapas, como describimos anteriormente: primero estenosis de la válvula tricúspide y creación de un defecto interatrial, y después, construcción del puente atriopulmonar con cierre completo de la válvula tricúspide. Después de cada etapa se obtuvieron angiocardiogramas.

Desafortunadamente, nuestras facilidades experimentales ac-

tuales no permiten obtener placas portables de animales recién operados, esenciales para detectar temprano complicaciones reversibles adversas al puente de injerto, tales como derrame pleural, neumotórax y otras.

Resultados

I. Estudios Hemodinámicos:

A. Tensión arterial

La tensión arterial sistémica promedio preoperatoria fue 179/100 mmHg. Al terminar la intervención, la tensión arterial varió considerablemente según los líquidos re-emplazados. El promedio fue de 92 sistólica, pero con re-emplazo, al devolver los animales a sus jaulas, la tensión promedio fue de 140/70. Al someterlos a cateterismo, los sobrevivientes tenían una tensión arterial promedio de 117/87.

B. Tensión en atrio derecho

Antes de cirugía, la tensión atrial derecha promedio fue de 8.5 cms. H₂O. Aumentó a 13 cms. después de abrir el puente atriopulmonar y se estabilizó en 9 cms. H₂O. Durante cateterismo la tensión en el atrio derecho era de 8 cms. H₂O.

C. Determinación de gases en la sangre

Se usó respiración artificial con presión positiva generada por oxígeno durante e inmediatamente después de la intervención quirúrgica. En forma consistente, los sobrevivientes demostraron valores para pO₂ arterial de 400 mmHg. o más. Los valores de pCO₂ arterial, entre 13 mmHg y 24 mmHg, al igual que para el pH arterial, de 7.410 y 7.593, reflejaron hiperventilación mecánica. Estos estudios se llevaron a cabo a intervalos variables desde el período inmediatamente postoperatorio a 4 días después de cirugía. Al determinarse la saturación de oxígeno venosa y arterial durante cateterismo, ésta fue 51 por ciento (SO_{2v}) y 88 por ciento (SO_{2a}), respectivamente.

D. Valores hemodinámicos (Figura 2)

Un cateterismo cardíaco llevado a cabo entre 4 y 10 meses después de la operación demostró los resultados promedios siguientes: gasto cardíaco 1.5 L/min. (1.24 a 1.83); índice cardíaco 2.4 L/min/m² (2.2 a 2.6); resistencia vascular pulmonar total 626 (480 a 712)

De la Sección de Cirugía Torácica y Cardiovascular, Sección de Cardiología y Departamento de Radiología del Hospital Municipal de San Juan y de la Escuela de Medicina de la Universidad de Puerto Rico.

Subvencionado por fondos donados por la Asociación Puertorriqueña del Corazón y por la Asociación Puertorriqueña para Investigación Médica (APRIM, Inc.)



Fig. 1: Muestra sondas cardíacas en posición para cateterismo completo derecho e izquierdo y determinación de gasto cardíaco, resistencia vascular sistémica y pulmonar, además de presiones intracardíacas.

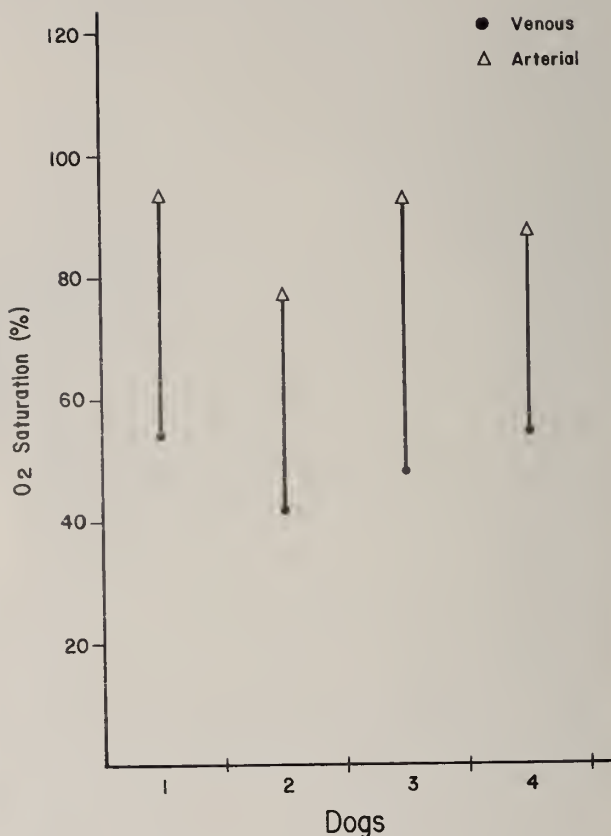
dinas/sec./cm⁻⁵, resistencia vascular periférica total 5220 (3840 a 5840) dinas/sec./cm⁻⁵; tensión pulmonar media 12 mmHg. (11 a 14) y tensión en ventrículo izquierdo al finalizar diástole 5 mmHg (1 a 8).

Estudios Radiológicos

Los estudios angiografiados confirmaron la permanencia del puente atriopulmonar a largo plazo. El material de contraste entró al atrio derecho, y casi de inmediato pasó por el homoinjerto a la arteria pulmonar, y de ahí al atrio y ventrículo izquierdo. Se demostró la normalidad del lado izquierdo y de la aorta (Figura 3).

En la mayoría de los animales operados la cantidad de material de contraste demostrada dentro del ventrículo derecho fue mínima. En algunos, algún escape de contraste al ventrículo ocurrió por aperturas diminutas en la válvula tricúspide, pero éstas cerraron con

O₂ SATURATIONS



Figs. 2A, B, C, D, E, F.: Muestran valores hemodinámicos y gases sanguíneos en sobrevivientes a largo plazo después de interposición de un puente atriopulmonar con homoinjerto de arteria y válvula pulmonar. 2A

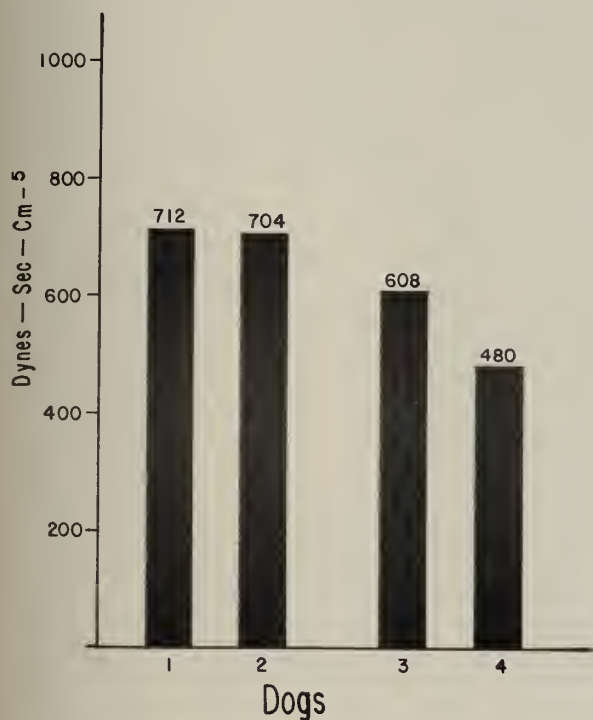
el tiempo. En otros, de más larga sobrevida, el homoinjerto aumentó en tamaño (Figura 4).

Un grupo de animales tuvo dos operaciones, primero, estenosis de la tricúspide y construcción de un defecto interatrial. Aquí fue fácil demostrar la estenosis, y por recirculación, la presencia del defecto. Luego, al finalizar la segunda etapa consistente en cerrar la tricúspide por completo y construir el puente atriopulmonar, pudo confirmarse la presencia del homoinjerto, abierto, sin trombosis.

Un animal murió aproximadamente tres semanas después de cateterismo cardíaco. El examen retrospectivo de las placas demostró entrada de la sonda al ventrículo derecho. Presumimos que al reabrir la válvula tricúspide el trauma recibido disminuyó el flujo sanguíneo a través del puente atriopulmonar y causó trombosis del injerto.

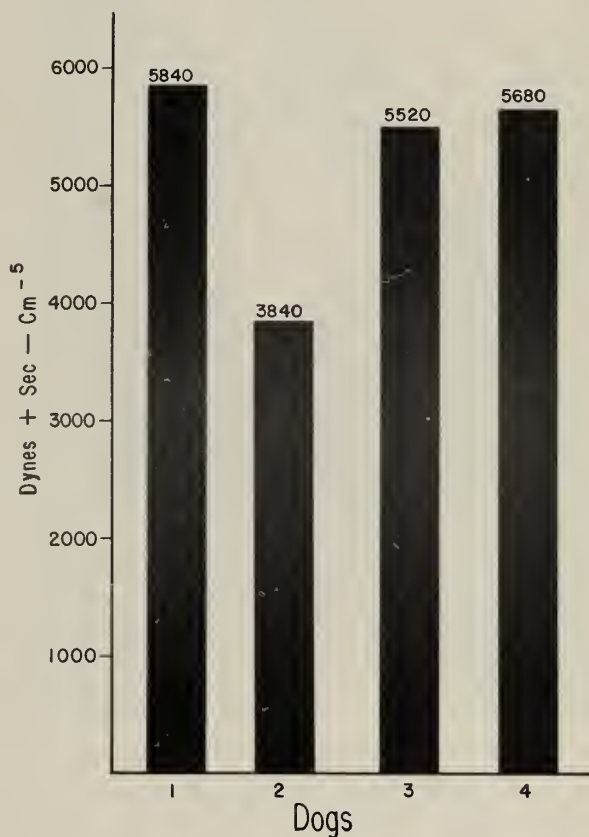
En ningún momento se demostró regurgitación del

TOTAL PULMONARY RESISTANCE



2B

TOTAL SYSTEMIC RESISTANCE



2C

injerto al atrio derecho a través de la válvula pulmonar del donante. El tamaño cardíaco de los sobrevivientes a largo plazo quedó sin alterarse.

Discusión

Presentamos una nueva alternativa a las intervenciones paliativas quirúrgicas, actualmente factible para aquellas anomalías congénitas que inutilizan la función del lado derecho del corazón, al afectar total o parcialmente la válvula tricúspide, la válvula pulmonar o el ventrículo derecho. Los resultados hemodinámicos a largo plazo apoyan la cautelosa aplicación clínica de esta nueva operación.

Las limitaciones de la anastomosis cavopulmonar fueron reconocidas desde la etapa investigativa. Graham y su grupo (2) confirmaron cuán letal era desviar ambas cavas, superior e inferior, a la arteria pulmonar. Ascitis y quilotórax aparecieron con disminución del flujo

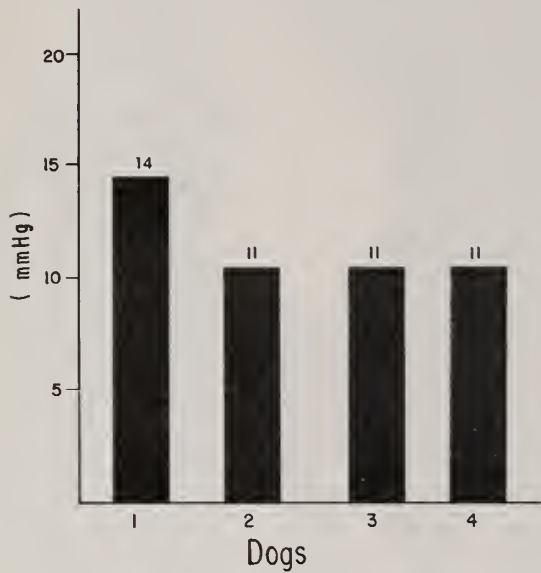
sanguíneo a través de la anastomosis.

De interés especial para aplicar esta operación es atresia de la tricúspide. Según Edwards y Burchell (3) en la forma más común de esta anomalía una estenosis subpulmonar la acompaña. Aunque el tronco pulmonar es de calibre menor que lo normal, su tamaño es adecuado para conducir el retorno venoso a los pulmones y permitir una anastomosis término lateral del injerto a la arteria pulmonar.

Hoy por hoy, los resultados a largo plazo de intervenciones paliativas, para atresia de la válvula tricúspide y otras anomalías asociadas o similares, no son satisfactorios. Los efectos adversos que acompañan el someter la arteria pulmonar a tensiones arteriales sistémicas, al construir una anastomosis de tipo Blalock-Taussig, Potts o Waterston, son bien conocidos y no se discutirán en detalle.

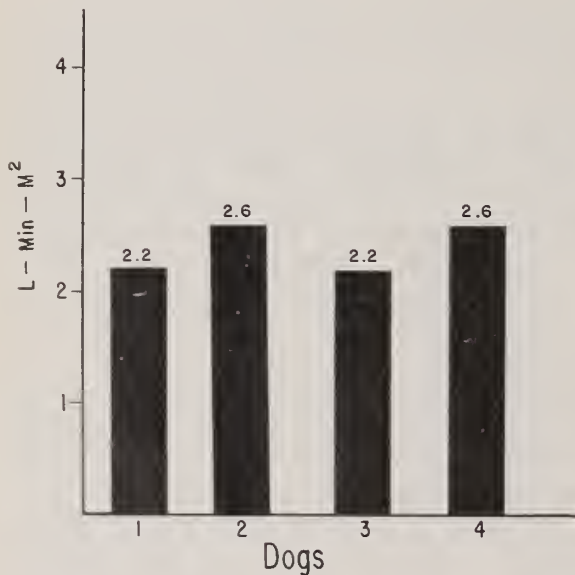
Más importante resulta considerar las complicaciones a largo plazo, y los resultados hemodinámicos de estu-

MEAN PULMONARY ARTERY PRESSURES



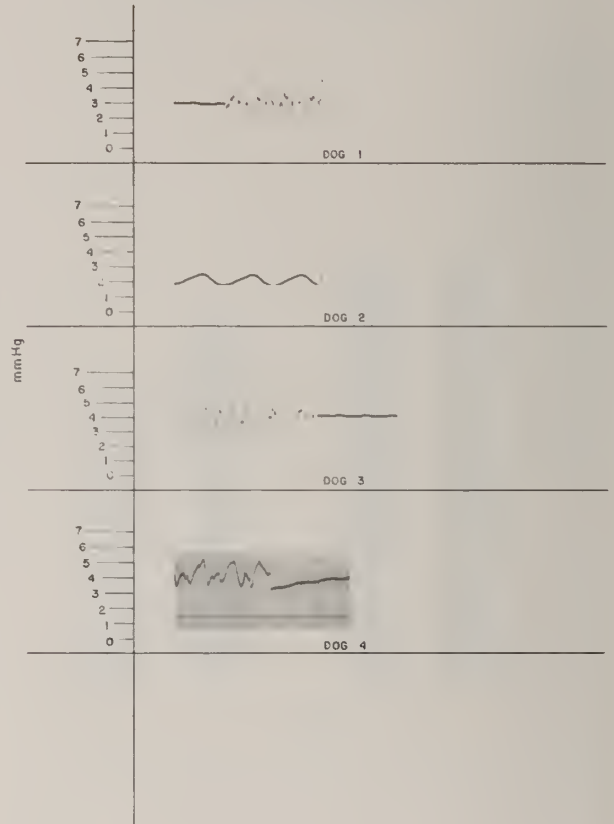
2D

CARDIAC INDEX



2E

RIGHT ATRIAL PRESSURES



2F

dios seriados después de anastomosis cavopulmonar, los cuales no han recibido la atención merecida. Según Calabrese y su grupo (4), 15 a 19 por ciento del flujo sanguíneo de la cava superior *llegaba al pulmón izquierdo*, por colaterales establecidas de la vena cava superior a la vena cava inferior en animales operados 4 a 11 años antes. Las arterias bronquiales se agrandaron y la circulación bronquial aumentó como resultado de una tensión pulmonar arterial derecha disminuída, por un lado, y debido a revascularización de trombosis pulmonares, por otro. Graham y otros (2) establecieron que 72 meses después, el flujo a través de una anastomosis cavopulmonar equivalía a 32 por ciento del gasto cardíaco, en realidad una disminución, porque se acepta que el pulmón derecho recibe normalmente una proporción mayor. La tensión pulmonar disminuyó en 50 por ciento, lo cual equivale a una estenosis pulmonar funcional y puede resultar en trombosis distal según observado por Naeye y su grupo (5).

Canent y otros (6) estudiaron 15 niños 18 a 30



Fig. 3: Angiocardiograma muestra un ventrículo izquierdo y aorta normales.

meses después de anastomosis cavopulmonar. La tensión en la arteria pulmonar derecha era de 10 a 15 mmHg. El gradiente a través del pulmón derecho (entre la arteria pulmonar y el atrio izquierdo) aumentó durante la diástole ventricular y disminuyó durante la sístole. Cualquier maniobra que aumentara la presión intratorácica aumentó este gradiente. Apnea y la maniobra de Valsalva (aumento sostenido en presión intratorácica) disminuyó el flujo sanguíneo. Igual resultado ocurre con atelectasis, pulmonía o compresión del pulmón por derrame pleural, según Young y Flemma (7), aunque aumenta el flujo sanguíneo durante el ejercicio (8). Estos datos explican nuestra incidencia de trombosis cuando ocurren tales complicaciones, por cierto, frecuentes en perros después de intervenciones torácicas, e imposibles de reconocer sin radiografías de tórax postoperatorias.

Martin y su grupo (9) relacionaron el nivel de hema-



Fig. 4: Angiocardiograma muestra material de contraste en vena cava superior, atrio derecho, e inmediatamente en la arteria pulmonar. Puede apreciarse el sitio donde un pequeño escape de material de contraste ocurrió al ventrículo derecho, por una apertura diminuta después de cerrada la válvula tricúspide quirúrgicamente; subsiguientemente esta apertura cerró por completo.

tocrito en el curso clínico postoperatorio y la tolerancia al ejercicio. La hipoxemia progresiva causa vasoconstricción pulmonar, aumenta la resistencia pulmonar y disminuye el flujo sanguíneo. Encontraron que después de anastomosis cavopulmonar a largo plazo se hizo necesaria otra intervención para aumentar la cantidad de sangre al pulmón izquierdo. Postulan ellos que el flujo a través de la cava superior, nunca más de un tercio del gasto cardíaco, es insuficiente para las necesidades metabólicas del niño en crecimiento.

¿Cuáles son las ventajas de un desvío atriopulmonar con injerto comparadas con una anastomosis cavopulmonar?

Primero, devuelve todo el retorno venoso al pulmón para oxigenarse con una saturación de oxígeno normal arterial. Segundo, debe minimizar las complicaciones tales como quilotórax y trombosis. Tercero, al desarrollar el atrio derecho hipertrofia muscular, quizás permita

sobreponerse a alzas mínimas en presión pulmonar arterial. Cuarto, obvia la necesidad a largo plazo de intervenciones adicionales. Quinto, permite cerrar la comunicación interatrial existente en estos casos y así disminuir el trabajo del corazón izquierdo. Sexto, la presencia de una válvula entre la circulación pulmonar y la venosa protege de insuficiencia y eorto eireuito de la sangre. En esencia, esta operación provee la corrección fisiológica total necesaria.

Quedan por determinar los resultados a largo plazo del uso de homoinjertos en niños, aunque ya éstos se aceptan para el tratamiento de troneo arterioso, tetralogía y atresia pulmonar (10) para comunicar el ventrículo derecho con la arteria pulmonar.

Los resultados hemodinámicos en estos experimentos reflejan una normalidad inesperada, en vista de prejuicios infundados sobre la esencia de la función del ventrículo derecho, y sostienen la interpretación nuestra: en el lado venoso y con integridad funcional del pulmón y del lado izquierdo, sólo se necesita una válvula en el sistema. Ciertamente, estos resultados apoyan la aplicación cautelosa de esta operación en humanos.

Por otro, y refiriéndonos al aspecto radiológico, nadie negará la importancia del angiocardiógrama en la evaluación pre y postoperatoria de lesiones cardiovasculares. Las combinaciones posibles de defectos congénitos relacionados con lesiones atrésicas del lado derecho del corazón son múltiples.

Con angiocardiógrafía, Kjellberg y su grupo (11) encontraron el atrio derecho, incluyendo la orejuela, agrandado en todos los casos de atresia de la tricúspide, con hipertrofia y dilatación. Es característicamente difícil de visualizar el ventrículo derecho, a menos que llene a través de una comunicación interventricular.

De acuerdo a Edwards (12) puede ser difícil diferenciar entre atresia tricúspidea y estenosis pulmonar. De ayuda son inyecciones diferentes de material de contraste, primero en el atrio izquierdo a través del defecto interatrial, seguido por inyección en el atrio derecho. En atresia tricúspidea el troneo pulmonar puede opacificarse si existe una comunicación interventricular, pero en atresia pulmonar la arteria pulmonar se opacifica por el ducto arterioso sólo después de opacificarse el arco de la aorta.

Ya ha habido algunos intentos clínicos en la dirección que apuntamos. Hurwitt (13) operó un niño cianótico de 4 meses con ventrículo único bajo el diagnóstico erróneo de atresia tricúspidea. Se unió la orejuela derecha a la arteria pulmonar, sin homoinjerto. Hurwitt advierte posibles desventajas del puente atriopulmonar:

1. fibrilación auricular puede disminuir la efectividad propulsora del atrio derecho.

2. descompensación del ventrículo izquierdo o enfermedad de la válvula mitral puede obliterar el gradiente entre atrio y arteria pulmonar y;

3. obliteración parcial de la arteria pulmonar puede limitar el volumen sanguíneo efectivo que el atrio derecho logre impulsar al atrio izquierdo.

Shumacker (14) interpuso un injerto entre el atrio derecho y la arteria pulmonar en un paciente con transposición de los grandes vasos. El paciente estuvo bien cerca de 8 horas, pero murió súbitamente sin que la autopsia explicara la causa de muerte. Ninguno de estos autores interpuso una válvula entre el atrio y la arteria pulmonar, lo cual creemos esencial.

En los últimos meses, sin embargo, ha habido intervenciones exitosas parecidas a la operación que proponemos. Arbulu y su grupo (15) extirpó la válvula tricúspide en drogadictos con endocarditis de esa válvula y logró sobrevivientes a largo plazo. Fontant y Bandet (16) llevaron a cabo en humanos una anastomosis cava-pulmonar derecha. Luego conectaron la orejuela derecha a la arteria pulmonar con un homoinjerto de válvula aórtica, y colocaron un homoinjerto de válvula aórtica a la entrada de la cava inferior al atrio derecho. Tienen ya tres sobrevivientes a largo plazo.

Circunstancias adversas, fuera de nuestro control, han impedido que ensayemos esta operación en humanos.

Resumen

Se llevaron a cabo estudios en sobrevivientes a largo plazo después de construido un puente atriopulmonar con homoinjertos de arteria y válvula pulmonar en perros con la válvula tricúspidea cerrada quirúrgicamente. La angiocardiógrafía mostró el paso de material de contraste por el atrio derecho, a través del injerto al pulmón y su regreso al corazón izquierdo. A largo plazo, el injerto dilató un poco.

El sondeo cardíaco demostró valores hemodinámicos dentro de los límites normales.

Estos resultados apoyan la aplicación clínica de esta operación, lo cual no ha sido posible hasta ahora por razones fuera de nuestro control.

Summary

Long term studies performed after atriopulmonary bypass in dogs with pulmonary valve and artery homograft revealed normal values during cardiac catheteriza-

tion and the unobstructed passage of contrast material through the right atrium, the atriopulmonar shunt, the lungs, left atrium and left ventricle. With time, the graft dilated somewhat.

These results support the clinical application of this operation, which has not been possible for us up to now.

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COMPARISON OF TWO VECTORCARDIOGRAPHIC LEADSYSTEMS (BURGER AND FRANK)

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From the very beginning of the electrocardiology, more than a half century ago, people have tried to form a physical model of the electrical activity in the heart. As a matter of fact, Einthoven, Farhr and De Waart (1913) worked with the concept of a heart muscle which propels electricity in an amount and direction that changes during the cardiac cycle. Figure 1 shows a schematic representation of the heart dipole located somewhere in the heart.

The curved lines are the pathways of the currents originating from the presence of the dipole in its conductive medium. Since the heart vector is changing continuously in size and direction, the head of the arrow that represents the vector, describes a spatial loop. The projections of this loop are recorded in vectorcardiography. We are aware that the dipole concept has many shortcomings from a theoretical point of view and that it can only serve as a crude description of the electrical activity in the heart muscle, however, it has proven to be useful as a diagnostic tool which is ample justification for its adaptation.

Once we have accepted the concept of a continuous changing dipole located somewhere in the heart, it follows that there exist linear relationships between the three components of the heart vector and the voltages that are produced by it at the surface of the body. Figure 2 shows a vector and its three components in the directions of the coordinate axes as they have been chosen in vectorcardiography. Below the figure you see the linear relationships between the vector components and the voltages at the surface of the body. Since the heart vector has only three components, H_x , H_y and H_z , only three equations are needed to determine the vector. In these equations appear at least three voltages, which can be recorded with a minimal number of four electrodes. These equations can have practical value, when the nine coefficients α_i , β_i , γ_i , three for each point on the surface of the body, are known. Since these

coefficients depend on anatomical and geometrical conditions and on electrical properties of different tissues between the electrodes and the heart, they can be determined experimentally with the aid of a model of the thorax which carries a known dipole instead of the heart. This was done for the first time during the Second World War by Burger and Van Milaan (1946, 1947, 1948) at the University of Utrecht in Holland. They used an *inhomogeneous* and *anisotropic* model of the thorax; inhomogeneous in order to account for different electrical properties of different tissues (muscles, lungs, bones); anisotropic since the conductivity depends on the direction in which the current flows. With their model they could not only determine the coefficients, but what is even more important, optimal positions for the electrodes. By optimal electrode positions we mean that we do *not* like to place electrodes on locations where a *minor shift of an electrode* will cause great changes in our results. The selec-

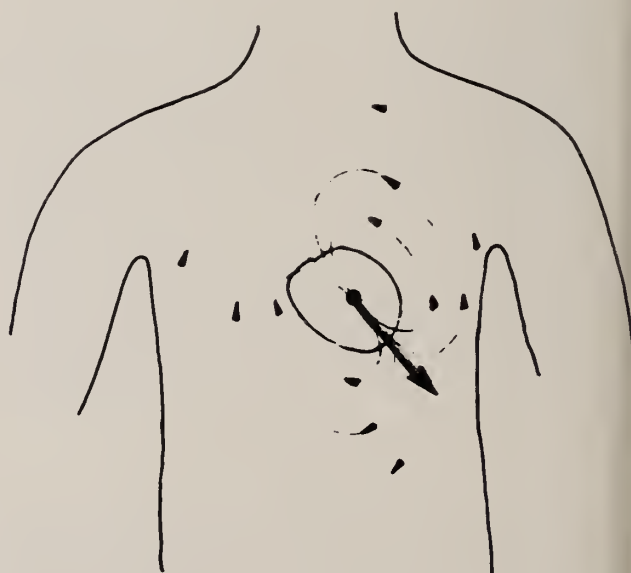


Fig. 1: Schematic representation of the heartdipole.

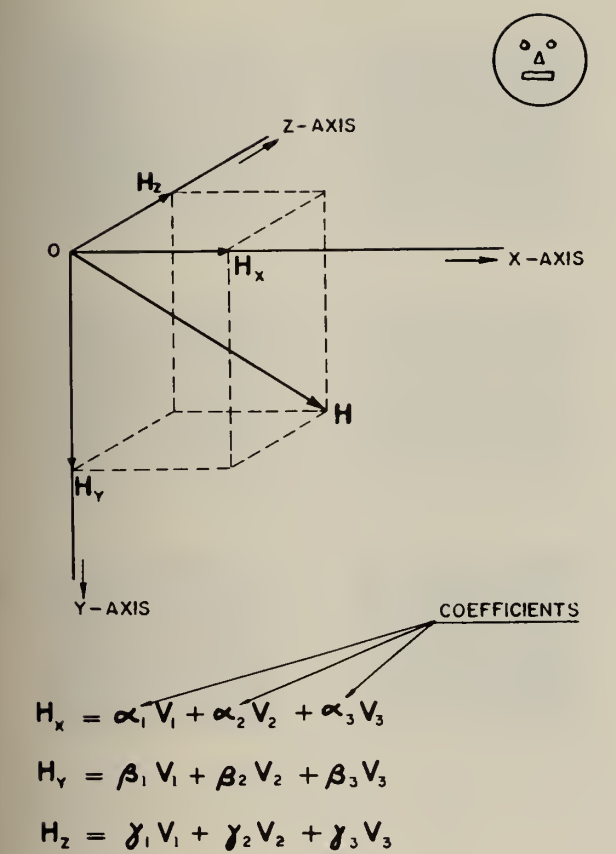


Fig. 2: Decomposition of a vector in three orthogonal directions.

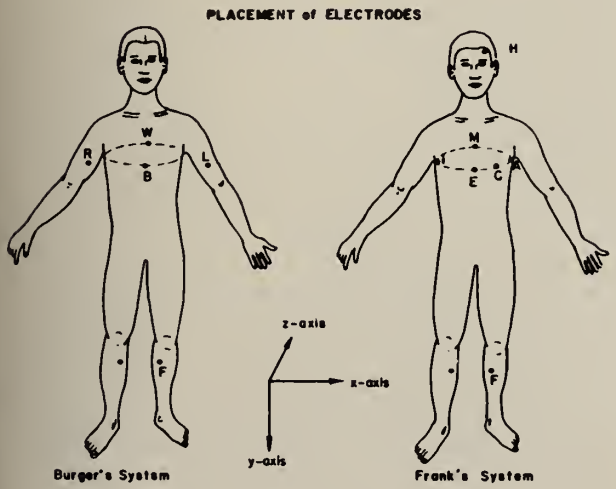


Fig. 3: Electrode positions of the Burger and the Frank leadsystem.

tion of the extremity leads by Einthoven, which are insensitive to electrode shifts, reflects the same philosophy. In this way, Burger and Van Milaan came up with a lead system of five electrodes, which is one more than the required minimum. Figure 3 shows the electrode positions of the Burger system.

One of the conditions that has to be fulfilled in order to justify the dipole concept is, that the distances from the electrodes to the heart are large when compared with the dimensions of the heart itself, see Burger, Van Brummelen and Van Herpen (1961). Since the body is rather flat, this condition is not fulfilled in the Z-direction; so an additional electrode, W, which can be looked upon as a correcting electrode for this shortcoming, was placed on the back.

The application of vectorcardiography has been hampered by the introduction of a great number of lead systems, most of them without a physical foundation, for they gave different results for the heart vector, due to the fact that the coefficients α_i , β_i , γ_i , which have been mentioned before, were not known. These coefficients were rather intuitively and arbitrarily chosen and the choices for the different systems were not interrelated. Other systems that have physical foundation, especially those in the United States, have been in use up to this date. However, while the latter systems have the advantage of giving similar results for the heart vector, they seem to compete for the greatest number of electrodes e.g. Frank (1956), Schmitt (1957), McFee, Rarungao (1961). It is not surprising, because of the similarity between the results of these systems, that the one with the smallest number of electrodes in this category, i.e. that of Frank, has found widespread use. The electrode positions of the Frank system are shown in figure 3. Since the coefficients of these systems were determined on homogeneous models, their loops differ from the loops obtained with the system of Burger, who used a more realistic model of the thorax. Those differences are not as significant as they appear to be, for as Burger (1957) pointed out, there exist simple mathematical relationships between the different systems. With a small correction in the vectorcardiograph very satisfactory similarity can be obtained between all systems, no matter where the electrodes are placed. It is just a matter of determining, once and for all, the correct coefficients on a proper model.

When we study results, obtained with any system, we have to realize that the quality of the results can never be better than those of the model on which the measurements are based. Thus if we, like it is actually done in vectorcardiography, take a model for the human

thorax, which has to serve as a model for an adult male as well as for an adult female, for obese as well as for skinny persons, and use the same model for children and newborns as well, then we have to be prepared to accept the limitations of such a model. We have to expect effects in our results which are not only related to the heart, but also to anatomical differences between our subjects. With these limitations in mind, it is obvious that a lead system, for general use in the clinic, based on a realistic model like that of Burger, cannot be improved by simplifying the model and then adding more electrodes; no matter how well the addition of electrodes can be defended on theoretical grounds for this simplified model. By doing this one puts a burden of extra routine work on the clinic, instead of relieving the clinic from useless work through the application of research done in a laboratory. Adding electrodes in this way is like putting a magnifying glass on a cheap watch, which might be five minutes slow or fast depending on several unknown conditions. What can be obtained in this way is a very accurate measurement of the wrong time. Addition of electrodes for a lead system to be used as a routine in the clinic should not be confused with research with multiple electrode systems, where one works with more sophisticated models.

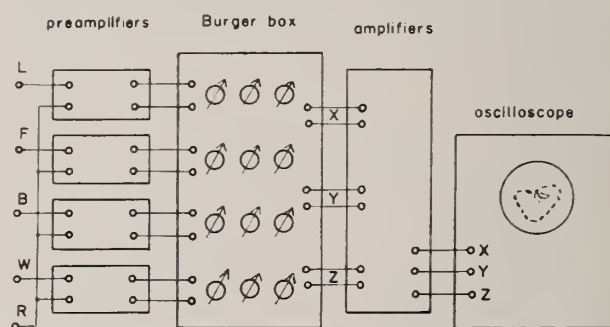
Figure 4, which shows vector loops of six subjects with normal hearts in the age group from 6 to 7 years, gives an impression about the deviations that exist between loops of subjects with normal hearts. Three projections of the spatial loop: frontal, horizontal and sagittal were recorded with the Frank lead system. The records are periodically interrupted at a rate of 1000 times per second; thus the distances between dots correspond with time durations of one millisecond.

When we compare the Burger lead system with that of Frank, with the aid of Figure 3, we see that the electrodes, which can be placed anywhere on the arms, have moved to the thorax to areas where minor shifts of the electrodes cause changes in the records. This is a great disadvantage especially for those, who work with small children that shift the electrodes by moving their arms. Another far more serious, disadvantage of the Frank system when compared with the Burger system, is the introduction of a so called "correcting electrode", C, also to be placed on the chest, between the front midline and left midaxillary line at an angle of 45° , not only because its location is difficult to determine, but also because it falls "somewhere" on, above, or under the breast of females. Since the layer of tissues between this electrode and the heart can vary 300 percent in thickness from one patient to the next, this electrode



Fig. 4: Vector loops of 6 patients with normal hearts in the age group from 6 - 7 years with the Frank lead system.

VECTORCARDIOGRAPH



BURGER BOX

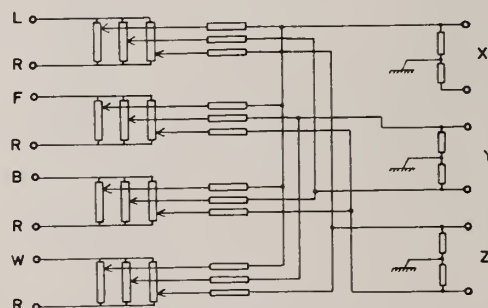


Fig. 5: Schematic representation of our vectorcardiograph with the Burger transformation box.

introduces uncertainties that outweigh the errors it might correct; briefly this is indicated by the term "unstable electrode". Finally, one has to apply a band around the head to put the last "correcting electrode". It was for the above reasons that we looked for a compromise between the Burger and the Frank lead system. We decided to use the Burger lead system for its optimal electrode positions, however, we sacrificed the correct coefficients by applying a transformation in order to obtain loops similar to the familiar loops obtained with the Frank lead system. This transformation is accomplished by a simple linear electrical network somewhere in the vectorcardiograph which will be discussed under methods.

In order to obtain a quantitative impression about the agreement between the transformed Burger loops and the Frank loops, we evaluated the agreement between the loops of 100 patients, which will be described under experiments.

Methods

As has been mentioned before, for a correct determination of the heart vector with a certain lead system, we have to know the coefficients $\alpha_i, \beta_i, \gamma_i$ in the linear relationships:

$$\begin{aligned} H_x &= \alpha_1 + \alpha_2 V_2 + \dots + \alpha_n V_n \\ H_y &= \beta_1 + \beta_2 V_2 + \dots + \beta_n V_n \\ H_z &= \gamma_1 + \gamma_2 V_2 + \dots + \gamma_n V_n \end{aligned}$$

where n is the number of measured voltages.

In the case of the Burger system there are only 4 voltages involved ($V_{LR}, V_{FR}, V_{BR}, V_{WR}$); the R electrode is used as a reference electrode; see figure 3. One of the consequences of the assumed linearity is that it should be possible to obtain the same result with a set of voltages obtained with another lead system, i. e. when the correct coefficients for that system are known. When for some reason we do not use the correct coefficients, we will obtain a result that looks different, however this incorrect result can also be produced with the Burger leads by a "proper" change of the coefficients. This change of the coefficients is accomplished by a so-called linear transformation. The effect of such a transformation on the shape of the loops can be seen in figures 6 and 7. Since the transformation is dependent on the anatomy of the subject and since we have to use the same transformation for all our patients, we have to work with an average transformation which will not give optimal results for all patients. However, from the degree of similarity that can be obtained for those subjects whose individual transformation is close to the average transformation, we obtain an impression as to what extent our assumption of linearity is justified. From figure 12 the reader can convince himself that the similarity is indeed very good. This high degree of similarity strongly suggests that in those cases where the similarity is not so great, we should have used other coefficients because those patients differ anatomically too much from the average. When this policy would

be followed, i. e. using different sets of coefficients for different types of patients, anatomical effects distorting the vector cardiogram would be eliminated. This procedure which is no burden for the clinician (with a selection knob on the vectorcardiograph a proper set of coefficients is selected before recording the vectorcardiogram) would result in smaller deviations between patients with similar heart conditions.

In order to show the interrelation between all lead systems, Burger *et al* (1962) determined from data collected from hundreds of patients the average transformation between the most important systems. With the aid of such a transformation we determined the coefficients that when used with the Burger leads will result in vectorloops similar to the loops one would obtain with the Frank lead system. This gave the following result:

$$H_x (\text{Frank}) = 27 V_{LR} + 16 V_{FR} + 1 V_{BR} + 2 V_{WR}$$

$$H_y (\text{Frank}) = -7 V_{LR} + 30 V_{FR} - 2 V_{BR} + 5 V_{WR}$$

$$H_z (\text{Frank}) = 9 V_{LR} - 13 V_{FR} - 16 V_{BR} + 33 V_{WR}$$

The solution of this set of equations is obtained with a simple linear network inside the vectorcardiograph. Figure 5 gives a schematic representation of our vectorcardiograph and the electrical network in the Burger transformation box. We used 12 variable resistors in the transformation network with which (3x4) coefficients, $\alpha_i, \beta_i, \gamma_i$, can be selected, which means that this box can also be used for any other transformation.

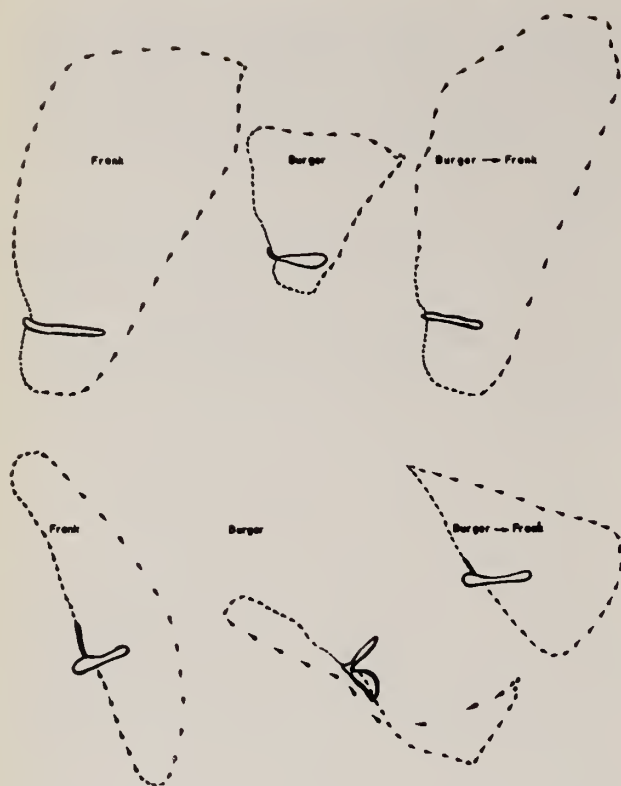
Since this paper is intended for the clinician, who usually has already a vectorcardiograph of his own, we do not go into the technical details of our setup. For those who would like to try this method, we advise to ask a manufacturer of vectorcardiographs to design an adaptation box with Burger leads with which the transformation can be accomplished.

The Burger leads are placed on the following positions: right arm (R), left arm (L), left leg (F), chest, a mid-sternal electrode placed at the level of the axillae (B) and back, 2 cm to the left of the seventh thoracic vertebra (W).

Material

In order to obtain a quantitative impression about the agreement between the transformed Burger loops and the Frank loops, we decided to evaluate the agreement between the loops of 100 patients (children from 4 to 9 years old). We recorded three projections of the spatial loop: horizontal, frontal and sagittal, with the transformed Burger and the Frank lead system with two vectorcardiographs. The line segments in the records are 1 msec apart and are as usual shaped like tear drops in order to be able to determine the direction in which the curves were described. In the Frank loops the blunt ends of the tear drops are leading, however, for the Burger loops we have the tail of the drops leading so that it is always possible to identify the system with which a vectorcardiogram was made.

Since mathematical similarity does not necessarily mean that the loops are clinically speaking similar and vice versa, we decided to use a subjective evaluation method, which is the one clinicians are using daily when they study vector



Figs. 6 and 7: The effect of the transformation on the shape of the loop.

loops. This method has been investigated by Burger *et al* (1964).

We asked four clinicians to evaluate the similarity between the loops by giving them grades from 1 to 10. In this scale stands:

- 10 for excellent
- 9 very good
- 8 good
- 7 more than sufficient
- 6 sufficient
- 5 doubtful
- 4 not sufficient
- 3 bad
- 2 very bad
- 1 no agreement

Results

Figure 6 shows the horizontal projections of a loop recorded with the Frank, the Burger and the transformed Burger system. The original Burger loop has changed due to the transformation; the agreement went about 2 points up in our grading scale.

Figure 7 shows the same thing for another patient. The Burger loop is twisted but the transformed loop is

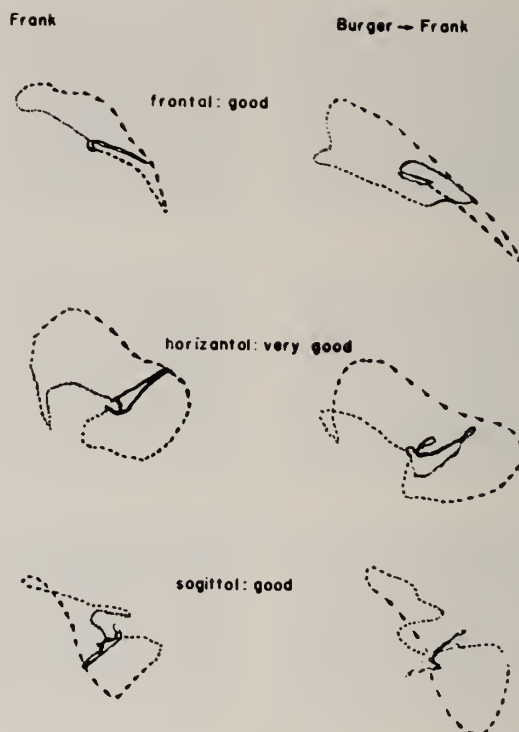


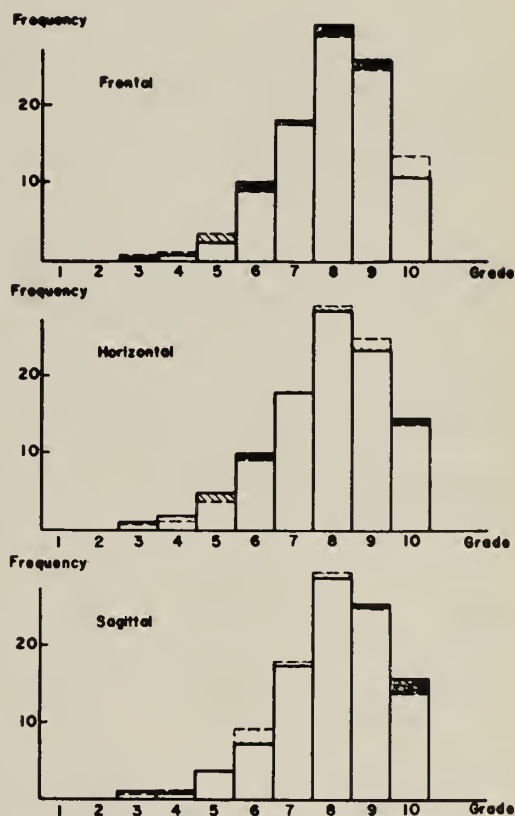
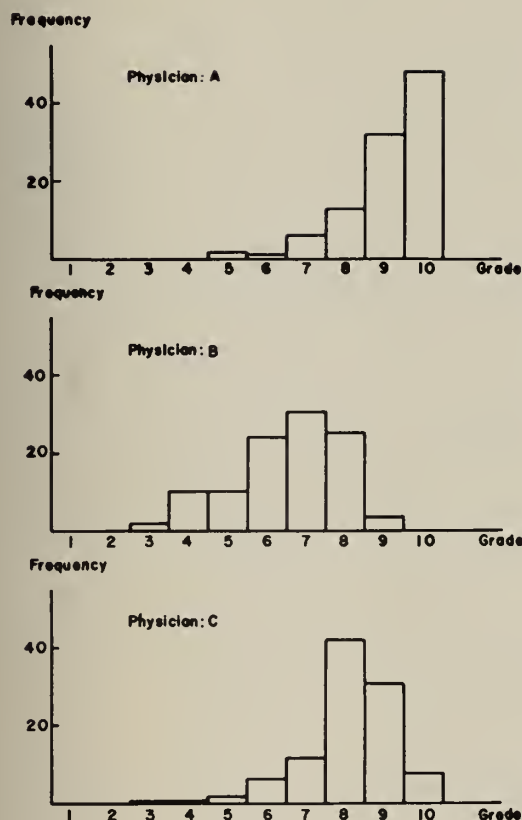
Fig. 8: Typical example of three projections of a vector loop recorded with the Frank and the transformed Burger system.

not. The agreement is not as good but went 2 points up in our grading scale due to the transformation.

Figure 8 shows a typical example of three projections of a vector loop recorded with the Frank and the transformed Burger system.

Since we used a subjective method to evaluate the agreement between the projections of the loops, one has to expect differences in the evaluation between different clinicians. In figure 9 we show the frequency distribution of the grades given by three different clinicians. For physician A, who gave the highest scores, lies the average around 9, which stands for very good. The average of physician B, who gave the lowest grades, lies around 7, which stands for more than sufficient agreement.

In figure 10 we show the frequency distribution of the grades given by all physicians together, to the separate projections: frontal, horizontal and sagittal. In order to facilitate the comparison of the different projections, we superimposed the average distribution (interrupted lines) on those of the individual projections. As can be seen, there is no statistical significant differ-



Figs. 9 and 10: Frequency distributions of grades given by different clinicians for the similarity between the vector loops and a comparison of the evaluation of separate projections.

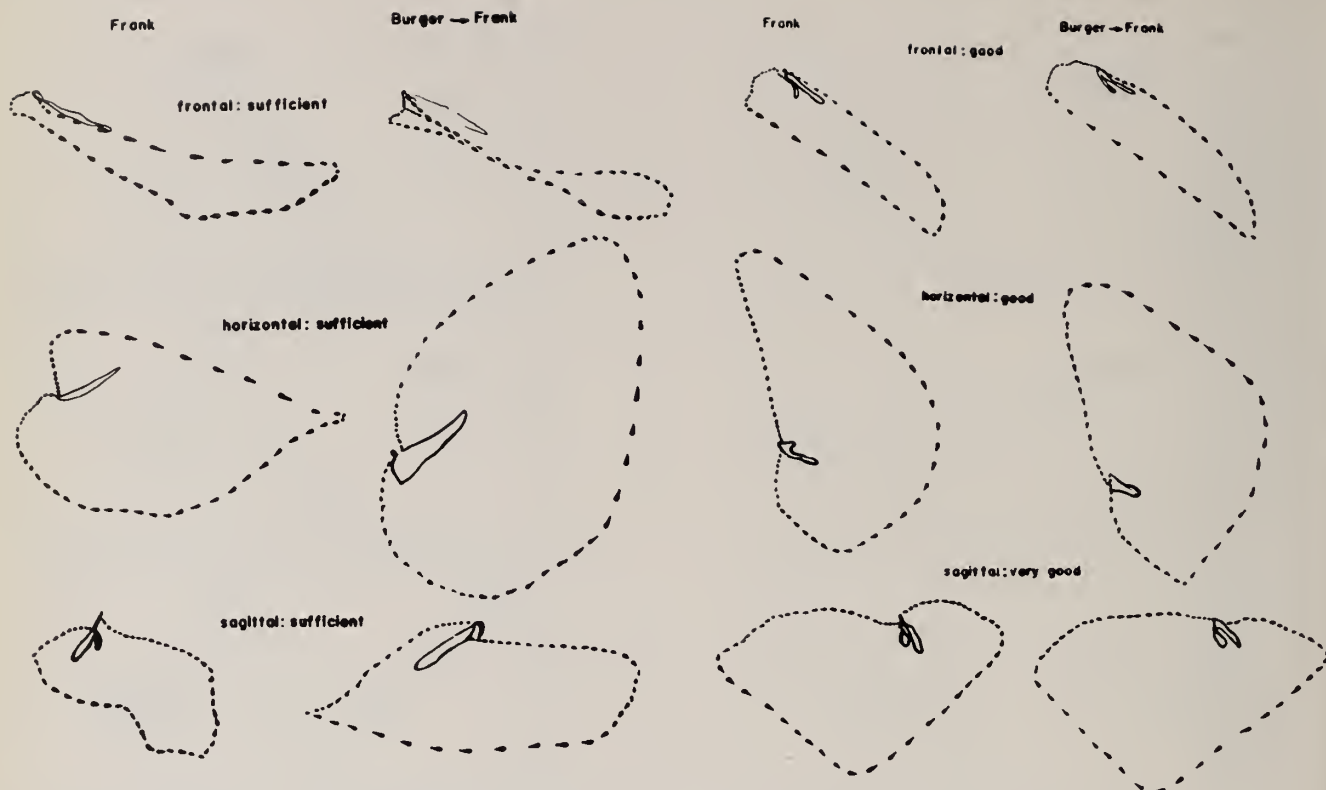
ce in agreement between the individual projections. The deviation from the average is shaded when the score of the individual projection is higher than the average and blank when the score is lower than the average. Since the shaded and blank areas cancel each other out, the difference between the individual projections is not only insignificant, but there is not even an indication that there might be a difference at all. This is very interesting, for it means that the failure of some limb electrode systems, with only one electrode on the thorax to render inaccurate horizontal projections has been corrected by one correcting electrode. Since there is not much left to correct for, the addition of still another correcting —but unstable— electrode at the same horizontal level is extremely difficult to understand.

In figure 11 we show one of the cases with less agreement between the Frank and the transformed Burger loops, however, in spite of this, the judges considered the agreement to be sufficient.

Figure 12 shows one of the better cases and it can be seen that there is no difference between the two systems whatsoever.

Since the determination of the level of the electrodes in the horizontal plane is sometimes difficult, we show in figure 13 as a very interesting case the records of a patient with a normal heart recorded with the electrodes placed at three different horizontal levels about 2.5 cm apart. We see that the changes in the loops are not so very great, however, the changes in the Burger loops are less than in the Frank loops. We remind the reader that these experiments were done on children where the disadvantage of the unstable Frank electrode is minimal.

Another interesting observation can be made by comparing the Frank loops from the upper level with the loops of both systems from the lowest level, for the agreement between the Frank loops and the Burger loops is better than the mutual agreement between the Frank loops.



Figs. 11 and 12: Similarity between the Frank and the transformed Burger loops.

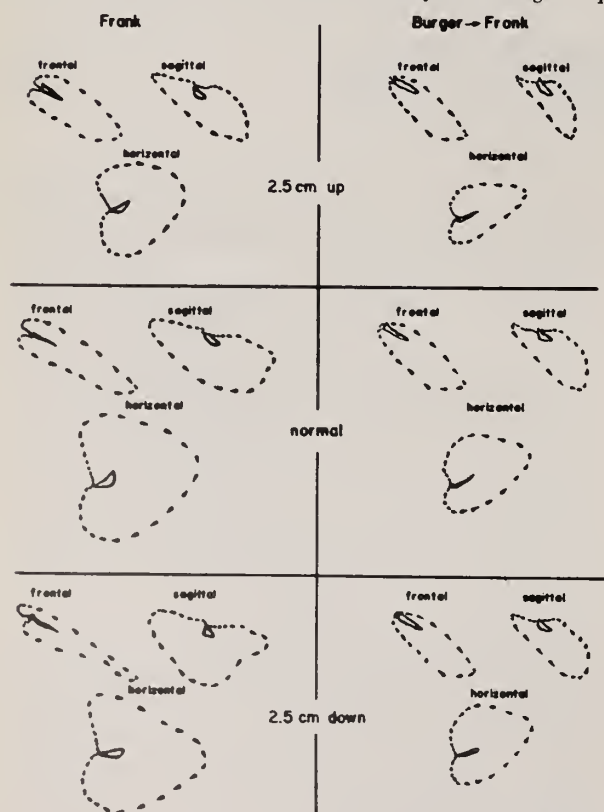


Fig. 13: The effect of electrode shift on the shape of the vector loops.

Summary

The practice of increasing the number of electrodes in order to obtain "improved" leadsystems for the clinic, which is defended by detailed theoretical analysis of crude models, cannot be justified when one does not account for anatomical differences between patients.

Improvements can be expected from several linear networks in the vectorcardiograph which enables the clinician to select different sets of coefficients for patients in different age-, sex-, and weight groups. These coefficients have to be determined once and for all on models or cadavers. The clinician can select the appropriate set of coefficients by turning a knob. By following this policy one adapts the models to reality and some of the effects on the vector cardiogram caused by anatomical differences between patients are removed.

The above indicates that the work in the clinic can substantially be reduced by using the Burger lead system with a transformation to Frank so that loops are obtained similar to the familiar Frank loops, while still the advantages of the greater accuracy of the Burger model and the optimal position of the Burger electrodes, absent in the Frank system, are retained.

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CONCEPTOS ACTUALES SOBRE LA ENDOCARDITIS INFECCIOSA

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La endocarditis infecciosa ha sufrido muchos cambios desde la introducción de los antibióticos. La mortalidad se ha reducido de un 99 por ciento (1) a un 17 por ciento en nuestros días (2). El agente etiológico, aunque en la mayor parte de los casos es todavía una bacteria, puede ser también un virus (3, 4), una rickettsia (5) o un hongo, (6, 7) de aquí que debe usarse el nombre de endocarditis infecciosa seguido por el del agente causal.

La cirugía cardíaca ha tenido su impacto sobre la enfermedad. Ha venido en ayuda de un grupo de pacientes que a pesar de mejorar del proceso infeccioso sucumbían poco después debido al daño mecánico ocasionado por la infección, especialmente a las estructuras valvulares del corazón (8, 9, 10, 11). En otros pacientes el proceso infeccioso no se ha curado hasta no hacerse la excisión quirúrgica del tejido infectado.

Incidencia

La endocarditis se presenta con mayor frecuencia en el adulto, especialmente en la quinta y sexta década de vida (3). La incidencia en la edad pediátrica es mucho menor; Blumenthal (12) menciona que en un hospital pediátrico grande constituyó un 0.5/mil de todas las admisiones. Las cifras dadas por Sinkford y Cassels (1) están de acuerdo con la anterior.

Naturalmente, la incidencia está condicionada por la frecuencia de las cardiopatías congénitas y reumáticas en el lugar, y la frecuencia de la cirugía. Esta última, como foco de entrada para infección y también por elevar el número de cardiopatías curadas quirúrgicamente. La profilaxis adecuada que se mantiene en los niños con cardiopatías y el tratamiento apropiado de las infecciones comunes disminuyen significativamente la incidencia de la endocarditis.

En los últimos dos años se han visto en el Hospital Universitario ocho pacientes con endocarditis. Dos de los niños tenían enfermedad cardíaca por fiebre reumática y seis por cardiopatía congénita (Tabla I).

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Etiología

El estreptococo y el estafilococo son responsables hasta en un 90 por ciento (2, 12, 13, 14) de los casos. El 10 por ciento restante puede ser causado por bacterias Gram negativas, (2, 12) infecciones mixtas, virus hongos y rickettsia. La endocarditis causada por organismos distintos al estreptococo viridans va en aumento (15). La naturaleza del organismo depende del sitio donde se ha originado éste, como por ejemplo, amigdalectomía, estreptococo; cirugía abdominal, enterococo. Es importante recordar la predilección del estafilococo áureo y la pseudomona por los pacientes hospitalizados.

Las cardiopatías predisponentes en pediatría son congénitas o reumáticas. Antiguamente predominaban las cardiopatías reumáticas (16), ahora la relación está invirtiéndose. De los 50 pacientes descritos por Zakrzewsky & Keith (17), 90 por ciento tuvieron cardiopatía congénita. Las condiciones que se complican más comunmente con endocarditis son el defecto interventricular, la tetralogía de Fallot, la estenosis aórtica, el ducto arterioso patente, la estenosis pulmonar y la coartación de la aorta (1, 12, 13, 17, 18). Cuando se trata de cardiopatías reumáticas, generalmente la lesión es de insuficiencia mitral o aórtica (12).

Diagnóstico

Las manifestaciones clínicas están divididas en tres grandes grupos. El primer grupo está constituido por signos y síntomas de infección sistémica severa, como son la fiebre, (1, 2, 12, 19) anorexia, decaimiento, sudoración, escalofríos y pérdida de peso.

El segundo grupo está formado por las manifestaciones embólicas. Estas se pueden localizar en la circulación pulmonar cuando provienen de lesiones del lado derecho del corazón y en la circulación sistémica cuando se originan en el lado izquierdo. Los órganos embolizados más frecuentemente son el bazo, los riñones y el cerebro (13).

El tercer grupo envuelve las manifestaciones del de-

TABLA I

Paciente	Edad	Cardiopatía	Entrada	Cultivo	Tratamiento	Resultado
1	5 años	Insuficiencia Mitral Congénita	Tracto Respiratorio	Negativo	Penicilina	Vivo
2	6 años	Pancarditis Reumática	?	Salm. D.	Ampicilina	Vivo
3	12 años	Ventrículo Común	?	Negativo	Penicilina	Vivo
		Atresia Pulmonar				
		Anastomosis Aortopulmonar				
4	11 años	Insuficiencia Mitral Reumática	?	Estreptococo Viridans	Penicilina	Fallecido *
5	16 meses	Insuficiencia Mitral Congénita	Tracto Respiratorio	Negativo	Penicilina	Vivo
6	12 años	Defecto Ventrículo Atrial (corregido)	?	Estafilococo Aureo	Penicilina Estafecilina	Vivo
		Válvula Tricúspidea Prostética				
7	5 meses	Comunicación Interventricular	?	Estafilococo Epidermidis	Penicilina	Vivo
8	3 años	Tetralogía de Fallot	?	Negativo	Penicilina	Vivo

NOTA: Los pacientes con cultivo negativo se trataron con penicilina inmediatamente después de tomar los cultivos. Tuvieron una respuesta clínica favorable a la penicilina y por esto no se les añadió otro antibiótico al no poder aislarse el organismo.

* Paciente no respondió a antibioterapia y sufrió reemplazo de válvula mitral durante etapa aguda; murió un mes después de la operación por un accidente cerebrovascular.

TABLA II: REGLAS PARA LA OBTENCION DE HEMOCULTIVOS

1. Tomar por lo menos 6 muestras en un lapso de 24 a 48 horas.
2. Cada muestra debe contener 5 cc. de sangre.
3. Deben ser obtenidas en condiciones asépticas.
4. No deben esperarse picos de fiebre para tomarlos.
5. Debe hacerse la siembra en medios aeróbicos y anaeróbicos o medios especiales cuando se sospeche un germen de terminado.
6. Deben tomarse antes de iniciarse el tratamiento con antibióticos.
7. Si el paciente tenía antibióticos antes de su ingreso deben suspenderse estos por 48 horas e iniciarse la toma de cultivos.
8. Si el paciente ha recibido penicilina se le debe añadir penicilinas a los medios de cultivo.
9. El laboratorio deberá retener el organismo aislado para determinar la acción bacteriana del suero y juzgar si el nivel de antibiótico en suero es adecuado.
10. En caso de no haber crecimiento en la muestra ésta no debe desecharse antes de 3 semanas.

terio en el estado cardíaco, como es la aparición del fallo congestivo. Actualmente, al contrario de lo que ocurría antes, la causa de muerte más frecuente no es la infección misma sino la insuficiencia cardíaca. Es importante recalcar que si se espera obtener los tres grupos de síntomas para hacer el diagnóstico, la enfermedad estará demasiado avanzada.

Otras manifestaciones como los nódulos de Osler,

las lesiones de Janeway, las hemorragias lineares y las petequias, generalmente se presentan tardíamente y hasta pueden encontrarse en pacientes con la enfermedad curada por varias semanas (13). Otro hallazgo importante en la serie de Blumenthal fueron las artralgias que se presentaron en el 24 por ciento de los niños (12).

Los datos de laboratorio incluyen una anemia leve o moderada, (12, 19) el mecanismo de la cual se cree que

TABLA III: NORMAS GENERALES PARA LA ANTIBIOTERAPIA

1. Debe iniciarse lo antes posible.
2. Debe usarse en dosis adecuada.
3. La elección del agente debe ser de acuerdo con el organismo aislado y las pruebas de sensibilidad *in vitro*.
4. Debe usarse por un tiempo adecuado: 6 a 8 semanas en casos de organismos resistentes, continuándose el tratamiento por lo menos dos semanas después de desaparecidos todos los signos de infección.
5. Deben preferirse los agentes bactericidas y nunca usarse los bacteriostáticos solos, aun cuando la selección se haya basado en la sensibilidad.
6. Debe iniciarse el tratamiento con dosis elevadas por vía endovenosa, divididas en dosis de 4 a 6 horas, durante por lo menos una semana.

sea una depresión transitoria de la médula ósea (1). La eritrosedimentación (12, 13, 16) está casi siempre elevada, puede haber leucocitosis e hipergamaglobulinemia. La prueba del factor reumatoide es positiva en un gran número de casos (60 por ciento de los pacientes de Weinstein) (13). La orina puede mostrar hematuria, albuminuria o francos signos de embolización renal, glomerulonefritis focal y en casos avanzados, insuficiencia renal (13).

El diagnóstico clínico precoz es muy importante. Friedberg ha demostrado que el promedio de recuperación fue significativamente más alto en los pacientes que recibieron tratamiento en las dos primeras semanas de haberse iniciado la enfermedad (2). En todo niño con cardiopatía y fiebre de origen desconocido se debe sospechar el diagnóstico de Endocarditis, diagnóstico que debe probarse con hemocultivos positivos los cuales deben hacerse en condiciones óptimas (Tabla II).

Con los hemocultivos tomados en estas condiciones se ha logrado recobrar el organismo hasta en un 83 por ciento de los casos (2). La mortalidad es mayor en aquellos pacientes en los que no se aísla un organismo.

La falla en recobrar el organismo se puede deber entre otras cosas a errores técnicos en la toma de la muestra, el uso indebido de los antibióticos, la endocarditis localizada en el lado derecho, y a períodos de remisión abacterianos cuando la enfermedad ha seguido un curso prolongado.

Tratamiento (Tabla III)

Para la endocarditis causada por el estreptococo viridans sensitivo a la penicilina se recomienda una dosis de 10 millones de unidades diarias por vía endovenosa, dividida en cuatro dosis. Blumenthal (12) aconseja usarla en esta forma por un período de una semana y después seguir con una combinación de penicilina cristalina y procainada en la dosis de 1 millón de unidades al día

por vía intramuscular, por un período de tres semanas.

Cuando las cepas de estreptococo son resistentes a la penicilina, hay que aumentar la dosis hasta 60 millones de unidades al día y combinarla con otro antibiótico al que el organismo sea sensitivo y que potencie la acción de la penicilina. Si se trata del enterococo (*estreptococo faecalis*) la mezcla de penicilina y estreptomina, o bien de penicilina con vancomicina es muy aconsejable. La penicilina debe usarse por vía endovenosa cada cuatro o seis horas ya que se ha demostrado que es mayor el grado de penetración cuanto mayor sea el nivel plasmático de la droga.

En los pacientes alérgicos a la penicilina, puede tratarse la desensitización, (20) tomando todas las precauciones, especialmente en aquellos con historial de reacciones graves. Se ha aconsejado el uso de esteroides, (21) pero se ha demostrado que aunque éstos suprimen las manifestaciones menores de intolerancia, no evitan el choque anafiláctico. Los antihistamínicos, que se han usado algunas veces, tampoco han resultado muy eficaces. Por estas razones es aconsejable recurrir a otros antibióticos como la lincomicina (21) y la cefalotina.

Cuando se trata del estafilococo que es resistente a la penicilina, se debe usar una combinación de penicilina en dosis muy alta y oxacilina, metilicina, nafcilina o vancomicina que son efectivos contra el estafilococo que segrega penicilinasas. La cefalotina, lincomicina, clorafenicol, eritromicina y rubramicina atacan las formas L del organismo y son otros antibióticos a considerarse (12).

El tratamiento de las infecciones por otras bacterias Gram positivas menos frecuentes depende de las pruebas de sensibilidad y de la respuesta clínica que se obtenga.

La endocarditis causada por gérmenes Gram negativos debe ser tratada casi siempre con combinaciones de antibióticos. Generalmente estas consisten de estreptomina, polomixina B, cloramfenicol, gamicina y carbenicilina, dependiendo de la sensibilidad del organismo

TABLA IV: FOCOS DE ENTRADA PARA LA ENDOCARDITIS INFECCIOSA

1. Infecciones orofaríngeas
2. Manipulaciones dentales
 - a) Con infección gingival
 - b) Sin infección gingival
3. Adenoamigdalectomía
4. Broncoscopía
5. Exploraciones rectosigmoidoscópicas
6. Exploraciones de vías urinarias
7. Infecciones cutáneas
8. Cirugía cardíaca (prótesis septales, valvulares, etc.)
9. Derivación ventrículo-auricular en hidrocefalos.
10. Marcapaso intracardíaco
11. Cateterismo cardíaco
12. Venodisección
13. Cirugía abdominal

**TABLA V: PROFILAXIS DE LA ENDOCARDITIS EN PACIENTES CARDIACOS
CON MANIPULACIONES OROFARINGEAS ***

1. Penicilina acuosa 600.000 unidades, combinada con penicilina procainada 600.000 unidades por vía intramuscular 2 horas antes del procedimiento para seguirse con penicilina procainada 600.000 unidades por vía intramuscular durante los dos días subsiguientes.
2. En caso de alergia a la penicilina, usar eritromicina 25 mgrs. por libra por día por vía oral por cuatro días empezando un día antes del procedimiento.
3. En pacientes cianóticos con hematocrito muy elevado penicilina acuosa un millón y medio de unidades diarias por vía intravenosa en suficiente cantidad de líquidos para evitar deshidratación, empezando dos horas antes del procedimiento y por un total de 3 días.
4. En casos de alergia a la penicilina en pacientes cianóticos se puede usar cefalotain 50 mgrs. por libra por día, administrada por vía intramuscular.

Cuando se van a realizar manipulaciones genito urinarias o gastro intestinales se debe agregar al regimen anterior estreptomicina 25 mgrs. por libra al día (sin exceder 1 gm. al día) o bien ampicilina 75 mgrs. por libra por día; ambas por vía intramuscular 2 horas antes del procedimiento y por un total de tres días.

* *Modificada de la rutina aconsejada por el Comité de Prevención de la Fiebre Reumática y Endocarditis Bacteriana de la Asociación Americana del Corazón - 28 - y usada en la Sección de Cardiología Pediátrica del Hospital Universitario.*

en vitro.

La infección causada por hongos, más comunmente por *Candida Albicans* tiene una mortalidad muy elevada. El tratamiento es anfotericina B, (6, 13, 23) droga muy tóxica y que debe manejarse con muchas precauciones.

Los pacientes con endocarditis y cultivos negativos, deben tratarse con combinaciones de antibióticos, como si se tratara de un organismo resistente (11, 12).

Además de los antibióticos, son necesarias las medidas de sostén como la hidratación, los antipiréticos y la digital. Se han usado los esteroides y agentes fibrinolíticos sin resultado alguno. También se debe mencionar que

en casos de embolización al anticoagulación está contraindicada.

Tratamiento Quirúrgico

En el 1940, Touroff y Vessel reportaron el primer caso de endocarditis bacteriana que no respondió a tratamiento médico y que se curó con la obliteración quirúrgica de un conducto arterioso patente.

Desde el 1965, con el empleo de la cirugía de corazón abierto se ha acumulado suficiente experiencia para justificar cirugía en la presencia de endocarditis, si las

lesiones hemodinámicas producidas por la destrucción del tejido cardíaco son incontrolables, (24, 25, 26, 27) como ocurre en la insuficiencia aórtica con fallo cardíaco. Algunas de estas lesiones son perforación de válvula, rotura de músculo papilar, perforación del septo interventricular, aneurisma y fístula del seno de Valsalva y embolia séptica.

Aunque contrario al concepto aceptado de no implantar cuerpos extraños en áreas infectadas, la mortalidad acumulativa de estas series fue de 33 por ciento. Esta mortalidad es muy aceptable cuando se considera que ella representa un grupo de pacientes seleccionados donde se creyó que el no operarlos hubiera sido uniformemente fatal.

Profilaxis

En pacientes reumáticos o con cardiopatías congénitas que van a ser sometidos a procedimientos quirúrgicos o manipulaciones que puedan ser foco de entrada para la endocarditis se debe usar antibióticos profilácticamente (Tablas IV y V). El uso de antibióticos disminuye la incidencia de infección al prevenir la bacteremia o reducir su magnitud (28, 29).

Pronóstico

Como se ha señalado anteriormente, el pronóstico ha mejorado dramáticamente con el uso de los antibióticos y la cirugía.

Entre los factores más importantes que determinan la gravedad y la evolución de la endocarditis pueden resumirse los siguientes:

1. La Sepsis
2. Las embolizaciones, tomando en consideración su localización y extensión.
3. Alteraciones cardíacas con:
 - a) Insuficiencia Cardíaca
 - b) Disfunción valvular
 - c) Pericarditis y taponamiento (30)

Resumen

Se presenta nuestra experiencia en los últimos dos años en el Hospital Universitario con ocho pacientes pediátricos con endocarditis.

Se hace hincapié en los cambios que ha sufrido esta enfermedad, en la etiología, manifestaciones clínicas y en su mortalidad. Es importante hacer un diagnóstico precoz e instituir tratamiento lo más pronto posible, tanto médico como quirúrgico. También se

aconseja el uso de la profilaxis a pacientes con cardiopatías que vayan a ser sometidos a cirugía o manipulaciones que puedan ser foco de entrada para la enfermedad.

Summary

Our experience in the past two years with eight patients admitted to the University Hospital with endocarditis is presented.

The changes in the etiology, clinical manifestations and mortality that the disease has undergone are emphasized. It is imperative that the diagnosis be made early and that treatment, both medical and surgical be instituted without delay. Prophylactic antibiotics are advised in patients with cardiac anomalies when they are subjected to procedures that may be portal of entry for infection.

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CARDIOPATIA CONGENITA SEVERA DEL RECIEN NACIDO

Análisis de 65 Casos de Autopsia

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Estadísticas recientes indican que la incidencia de Cardiopatías Congénitas en el recién nacido es alrededor del .82 por ciento (1), la incidencia en la edad escolar es de .48 por ciento (2); esto sugiere que una de las causas más importantes para esta reducción es una mortalidad elevada. La mayor parte de las muertes se produce en el primer año de vida y especialmente en el período neonatal pues se estima que hasta una tercera parte de ellos, mueren en esta etapa (3). Muchos de estos pacientes son salvados si se diagnostican precozmente y se tratan de emergencia.

Los grandes cambios hemodinámicos que se producen después del nacimiento hacen que un diagnóstico correcto y temprano a esta edad sea un verdadero reto tanto para el Cardiólogo Pediatra como para el Pediatra General.

El cuadro clínico de estos pacientes está influenciado por tres condiciones que son inherentes a la primera semana de vida (4, 5, 6, 7) y las cuales van desapareciendo a medida que el neonato crece y son:

1. El conducto arterioso que se contrae y se cierra funcionalmente pocas horas después del nacimiento puede en condiciones patológicas como la hipoxia o la acidosis permitir un cortocircuito de izquierda a derecha o de derecha a izquierda.
2. La hipertensión pulmonar disminuye después de iniciada la respiración haciendo que aumente el flujo pulmonar.
3. El cierre del foramen ovale se debe a que el retorno venoso pulmonar aumenta en el nacimiento elevando la presión del atrio izquierdo, por encima de la del atrio derecho.

Todos estos ajustes, se completan hacia la sexta semana postnatal.

El propósito de este artículo es el de revisar nuestro material de autopsia correspondiente a recién nacidos

con cardiopatía congénita, con el objeto de determinar la incidencia de malformaciones cardíacas letales en este período, discutir sus formas de presentación, diagnóstico y tratamiento.

Material y Métodos

Se revisaron los expedientes de todos los pacientes cardíacos que se presentaron con cardiopatía severa en el período neonatal y que murieron en las primeras seis semanas de la vida. La cardiopatía ocasionó la muerte o bien fue un factor determinante mayor. Se incluyen solamente los casos que tuvieron autopsia desde enero de 1968 hasta octubre de 1971 (Tabla I).

Los 65 pacientes que se discuten no reflejan la incidencia real de cardiopatías severas en Puerto Rico en vista de que nuestro material es seleccionado por ser el Hospital Universitario un centro de referimiento.

Los casos descritos representan diversas cardiopatías; la edad en que se admitieron varía desde los que nacieron en el hospital hasta los que ingresaron a las cuatro semanas de edad.

A la mayoría de estos pacientes se les hizo cateterismo cardíaco, cirugía o ambos, pero hubieron algunos que por razones diversas no tuvieron los procedimientos indicados. Se hizo en todos ellos una evaluación clínica, incluyendo la radiografía de tórax y el electrocardiograma.

Aunque los recién nacidos con cardiopatía congénita severa se presentan ya sea con signos de hipoxia, de insuficiencia cardíaca o ambos, se describen las malformaciones en orden de frecuencia y se discuten sus formas típicas de presentación.

Atresia Aórtica

Esta anomalía fue la más común en nuestra serie, pues se presentó en 12 pacientes (8 mujeres y 4 varones). Generalmente está acompañada de atresia mitral, hipoplasia de la aorta ascendente y del ventrículo izquierdo. En casos menos severos existe una comunicación inter-ventricular y una válvula mitral más o menos adecuada (8, 9). Para que estos pacientes puedan sobrevivir deben tener una comunicación interauricular que permita un cortocircuito de izquierda a derecha y un conducto arterioso de buen calibre que pueda suplir en forma adecuada la circulación sistémica y coronaria.

Todos estos pacientes, excepto uno, estuvieron muy graves y murieron en la primera semana de vida. Se presentaron con insuficiencia cardíaca congestiva, ta-

TABLA I: MATERIAL DE ESTUDIO

Cardiopatía	No.Pacientes	Porcentaje
Atresia Aórtica	12	18.5
Transposición de los Grandes Vasos	11	17.0
Coartación de la Aorta	10	15.4
Comunicación Interventricular Complicada	9	13.8
Corazón derecho hipoplástico	6	9.2
Atresia Tricuspídea	5	7.7
Canal Atrio-ventricular	4	6.1
Anomalías Cardíacas Complejas	3	4.6
Tronco arterioso	2	3.1
Estenosis o Atresia pulmonar	2	3.1
Estenosis Aórtica	1	1.5
Total -	65	100.0

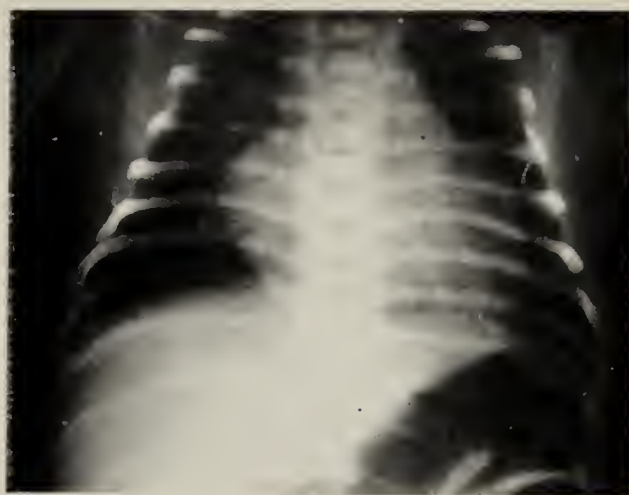


Fig. 1: Radiografía de tórax que demuestra cardiomegalia con marcada congestión venosa.

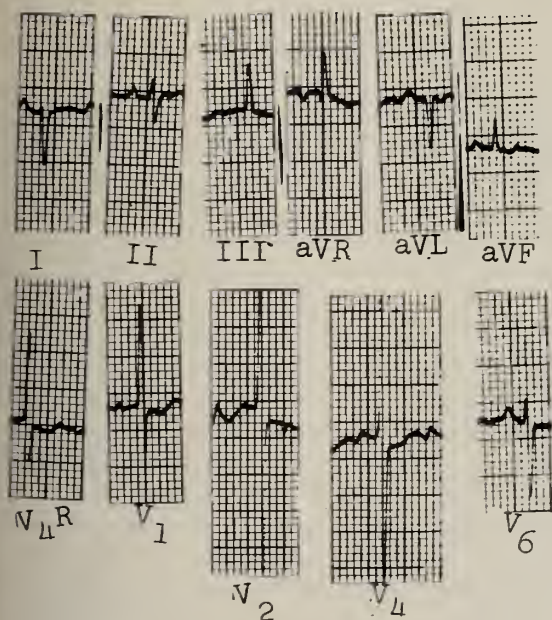


Fig. 2: Electrocardiograma de un paciente con corazón izquierdo hipoplástico mostrando preponderancia de ventrículo derecho y disminución de los voltajes del ventrículo izquierdo.



Fig. 3: Angiograma en el que se observa hipoplasia de la aorta ascendente en fase tardía con una inyección en la arteria pulmonar.

quipnea, cianosis y pulsos débiles; sólo uno de nuestros pacientes tuvo buenos pulsos debido a un conducto arterioso grande. Todos presentaron un segundo sonido sencillo y ocho tuvieron soplo.

La radiografía de tórax (Fig. 1) mostró cardiomegalia

significativa con marcada congestión pulmonar venosa en todos los pacientes. El electrocardiograma (Fig. 2) se caracterizó por una hipertrofia ventricular derecha con disminución de los potenciales del lado izquierdo; solo un paciente mostró hipertrofia biventricular; siete



Fig. 4: Radiografía de tórax mostrando corazón de forma ovoide, cardiomegalia, pedículo estrecho y vascularidad aumentada.

presentaron además, agrandamiento de atrio derecho.

Como todos estos pacientes están tan críticamente enfermos, no es posible realizar en ellos estudios completos de cateterismo (10). Lo que se encuentra en estos estudios es un cortocircuito de izquierda a derecha a nivel atrial y presiones muy altas en el atrio izquierdo. Las presiones son sistémicas en el ventrículo derecho, en la pulmonar y en el conducto arterioso.

El angiograma (Fig. 3) cuando se inyecta en la pulmonar muestra en la fase tardía opacificación del atrio izquierdo y no del ventrículo izquierdo ni de la aorta ascendente. La aorta se opacifica retrógradamente y se muestra hipoplásica.

Es poco lo que se le puede ofrecer al paciente desde el punto de vista terapéutico, ya que no responden a las medidas anticongestivas. Se han descrito últimamente con resultados pobres, operaciones tendientes a mejorar el flujo sistémico y disminuir el flujo pulmonar (11), en primer lugar se debe ampliar la comunicación interauricular, luego se debería hacer una constricción quirúrgica de las arterias pulmonares. Hasta el presente no hemos intentado ninguno de estos procedimientos.

El exámen patológico del corazón mostró atresia aórtica con hipoplasia de la aorta ascendente en todos los pacientes; en nueve de ellos el ventrículo izquierdo era hipoplástico, en los tres restantes había un defecto interventricular lo que hacía que el ventrículo izquierdo no fuese tan diminuto y sólo uno presentó una comunicación interauricular adecuada. Este último fue el único que sobrevivió hasta el mes de edad.

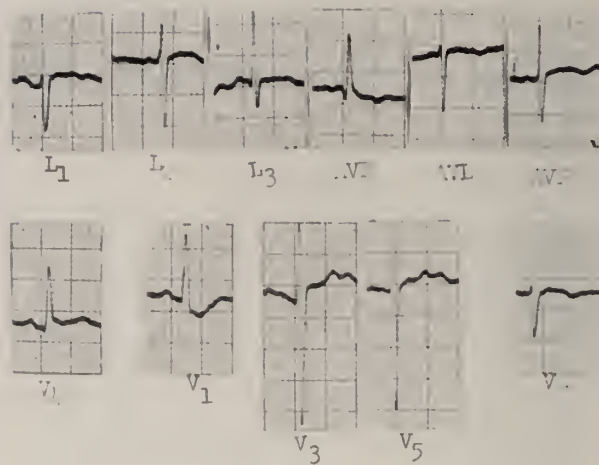


Fig. 5: Electrocardiograma con eje a la derecha e hipertrofia ventricular derecha.

Transposición de los Grandes Vasos

Este defecto en el que la aorta sale del ventrículo derecho y la pulmonar del ventrículo izquierdo, necesita de una comunicación entre ambas circulaciones para ser compatible con la vida, generalmente es la comunicación interauricular. Después de la atresia aórtica, fue el defecto más común entre nuestros pacientes, 11 de 65 pacientes, 7 hombres y 4 mujeres. Cuando la transposición es con septo interventricular intacto los síntomas aparecen generalmente en la primera semana de vida y son los de hipoxia con cianosis severa e hiperepnea. En cambio, si hay un defecto interventricular los problemas empiezan después y son de insuficiencia cardíaca, siendo la cianosis menos intensa.

De nuestros 11 pacientes, 7 tuvieron septo interventricular intacto y se presentaron con cianosis desde el nacimiento. De los cuatro con defecto interventricular todos desarrollaron insuficiencia cardíaca, pero sólo dos presentaron cianosis desde el nacimiento. Los 11 pacientes tuvieron soplo cardíaco y 6 tuvieron un segundo sonido sencillo.

La radiografía de tórax (Fig. 4) tiene características especiales como son la forma en huevo de la silueta cardíaca, cardiomegalia, pedículo estrecho y aumento de la circulación pulmonar. Sin embargo, estos hallazgos no se presentan en todos los pacientes, especialmente, en la primera semana de vida.

El electrocardiograma (Fig. 5) es variable, el eje de nuestros pacientes estaba desviado a la derecha en 7

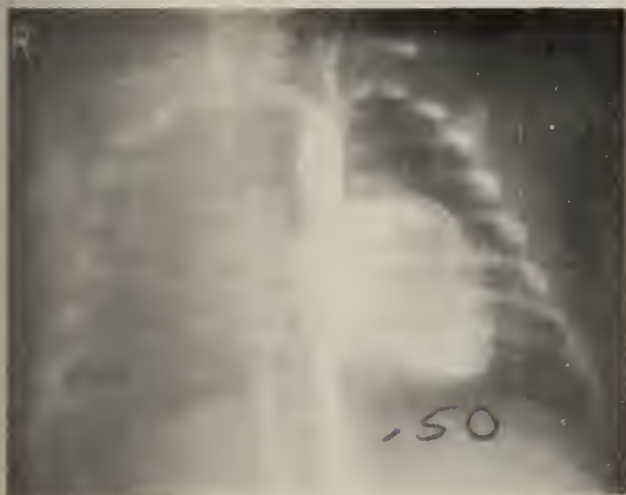


Fig. 6-A: Angiocardiograma de ventrículo derecho en posición P-A mostrando la emergencia de la aorta de esta cavidad y en posición alta; no hay defecto interventricular ni conducto arterioso patente.



Fig. 6-B: Angiocardiograma de ventrículo derecho en posición lateral dando origen la aorta en posición alta y anterior.

y a la izquierda en 4, había hipertrofia ventricular derecha en todos excepto uno en el que existía hipertrofia biventricular. Generalmente los casos que tienen defecto interventricular presentan a la larga hipertrofia biventricular. Se encontró agrandamiento de ambos atrios en un paciente.

Cuando existe la sospecha clínica de transposición en un recién nacido debe realizarse el cateterismo cardíaco para probar el diagnóstico y las anomalías asociadas que frecuentemente son: el defecto interventricular, el conducto arterioso patente y la estenosis pulmonar. Uno de los objetivos principales del cateterismo es el de evaluar el tamaño de la comunicación interauricular. El estudio hemodinámico muestra un cortocircuito de izquierda a derecha a nivel atrial y también a nivel ventricular si hay comunicación interventricular. La presión en el ventrículo derecho que es el que da origen a la aorta está a nivel sistémico. El diagnóstico se confirma con un angiograma de ventrículo derecho que muestra la aorta saliendo de este ventrículo en posición alta y anterior (Figs. 6A y B). Esta inyección también permite ver si hay comunicación interventricular o conducto arterioso patente.

Cuando la comunicación interauricular no es adecuada ésta debe ampliarse con una septostomía de balón descrita originalmente por Rashkind (13) y que consiste en introducir un catéter de balón desde el atrio derecho al izquierdo, inflar el balón en esta posición y jalar brus-

camente hacia el atrio derecho rompiendo el septo interauricular. Cuando este procedimiento tiene éxito, mejora la mezcla entre las dos circulaciones, además se descomprime el atrio izquierdo, disminuyendo así la hipertensión pulmonar (14). De nuestros 11 pacientes, 2 tuvieron septostomía de balón y cuatro la operación de Blalock-Hanlon que consiste en crear un defecto interatrial quirúrgicamente.

En un paciente con estenosis pulmonar severa fue necesaria la operación de Potts.

El tratamiento médico a estos pacientes consistió en digital y oxígeno, además de bicarbonato de sodio para la acidosis.

Coartación de la Aorta

El síndrome de la coartación de la aorta se presentó en 10 pacientes que junto a las dos anomalías anteriormente descritas constituyó más de la mitad de los pacientes; cifra que concuerda con otros autores (15). Casi todas las coartaciones tuvieron defectos asociados, el conducto arterioso estuvo patente en todos los pacientes. Cinco tuvieron una comunicación interventricular y uno, una comunicación de ventrículo izquierdo a atrio derecho. La presencia de anomalías cardíacas asociadas es la causa del fallo cardíaco temprano. La principal característica de esta entidad es la diferencia en la intensidad de los pulsos y las presiones entre las



Fig. 7: Radiografía de tórax que muestra cardiomegalia y marcada congestión de tipo venoso característica de fallo cardíaco.



Fig. 9: Aortograma demostrando el segmento coartado.

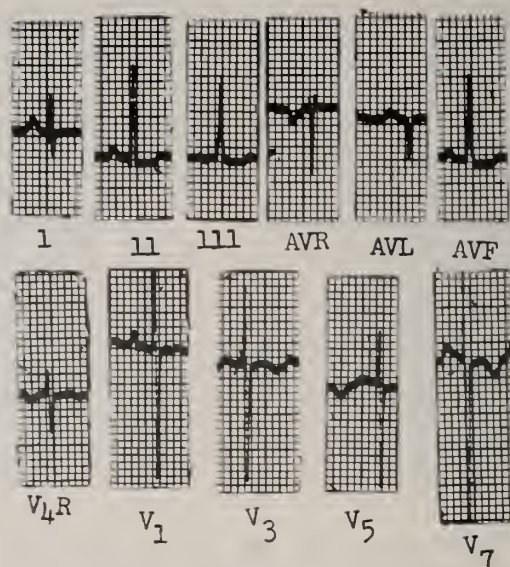


Fig. 8: Electrocardiograma que presenta hipertrofia ventricular derecha y posiblemente izquierda.

extremidades superiores y las inferiores; sin embargo, esto depende del tamaño del conducto arterioso. En nuestro grupo de pacientes sólo uno tuvo pulsos que se consideraron normales, en el resto, los pulsos estaban disminuídos en las piernas y en un paciente estaban ausentes. Es frecuente que estén cianóticos (16) como sucedió con 50 por ciento de los casos. La mayor parte de ellos presentaron soplo y un segundo sonido fuerte a expensas del componente pulmonar.

Las radiografías de tórax (Fig. 7) mostraron cardiomegalia considerable con la congestión venosa característica del fallo cardíaco. El electrocardiograma (Fig. 8) mostró invariablemente hipertrofia ventricular derecha asociada en ciertos casos, con hipertrofia ventricular izquierda, sólo uno no presentó hipertrofia de ninguna de las cavidades. El cateterismo cardíaco además de reconocer la variedad de la coartación, descubre las anomalías asociadas. Se encuentran cortocircuitos en los casos que tengan comunicación interventricular. Generalmente las presiones y las oximetrías son diferentes en la aorta ascendente y la descendente. En los casos no complicados se hace en nuestro hospital un aortograma utilizando la arteria carótida común, lo que permite una visualización clara de la porción coartada (Fig. 9).

El tratamiento de las coartaciones en nuestro servicio es siempre inicialmente médico con digital, diuréticos, oxígeno, etc. Algunos de los pacientes responden rápi-

damente, otros no, o bien responden inicialmente y después se deterioran. A estos últimos los observamos cuidadosamente por unas pocas horas y si las medidas médicas no son suficientes se considera la cirugía rápidamente. La mortalidad quirúrgica es alta antes de los seis meses de edad, pero ésta depende directamente de la severidad y la longitud del segmento coartado y de las anomalías asociadas (17). De nuestros 10 pacientes se operaron 8 y en todos ellos se trató de corregir la coartación y hacer constricción quirúrgica de la arteria pulmonar si tenían comunicación interventricular grande. Cuando había un conducto arterioso éste fue ligado al mismo tiempo.

Defecto Interventricular

Nueve de nuestros pacientes tuvieron comunicación interventricular. En uno se encontraron defectos musculares múltiples, cuatro tuvieron además conducto arterioso, y en cuatro conducto arterioso y comunicación interatrial. En todos ellos la lesión predominante fue el defecto interventricular.

Los recién nacidos que tienen sólo comunicación interventricular no se presentan generalmente con síntomas graves, en la mayoría el soplo aparece entre las 3 y 6 semanas. Hay casos en los que la resistencia pulmonar cae precipitadamente, el cortocircuito de izquierda a derecha es enorme y los pacientes se van en fallo cardíaco (16) y pueden morir en edema pulmonar en edad muy temprana.

Todos nuestros pacientes tuvieron soplo, fallo congestivo y presentaron un segundo ruido aumentado a expensas del componente pulmonar.

La radiografía de tórax se caracterizó por cardiomegalia con silueta cardíaca inespecífica y vascularidad pulmonar que fue aumentando con la edad del paciente.

El electrocardiograma muestra casi siempre hipertrofia biventricular, sino inicialmente, con el correr de los días. La mayor parte de nuestros pacientes desarrollaron hipertrofia ventricular derecha y sólo uno presentó hipertrofia ventricular izquierda. Dos presentaron agrandamiento de atrio derecho. El eje fue de $+120^\circ$ en seis pacientes e indeterminado en uno.

El cateterismo cardíaco demuestra el defecto interventricular y las anomalías asociadas. Como el foramen ovale está patente en casi la totalidad de estos pacientes, es relativamente fácil llegar al ventrículo izquierdo para allí hacer las inyecciones del contraste. Cuando no hay respuesta al tratamiento médico in-

tenso, hay que acudir a la constricción quirúrgica de la arteria pulmonar (18, 19, 20) y ligar el conducto arterioso.

Corazón Derecho Hipoplástico

Tuvimos 6 casos de corazón derecho hipoplástico. Todos ellos se presentaron con cianosis temprana y dificultad respiratoria. La mayoría tenía soplo y presentaba flujo pulmonar disminuido a la radiografía. Todos presentaron hipertrofia de ventrículo izquierdo y tres de ellos atrio derecho agrandado.

En el cateterismo se confirmó la hipoplasia de ventrículo derecho y los defectos asociados que fueron defecto interventricular, estenosis pulmonar, conducto arterioso, defecto interatrial y canal atrioventricular común; en todos ellos la válvula tricúspide era pequeña. Se trató de aumentar el flujo pulmonar con anastomosis quirúrgicas aortopulmonares en tres pacientes.

Atresia Tricuspea

La serie tiene 5 pacientes con atresia de la válvula tricuspea, la cual siempre está asociada a otros defectos (22), de otro modo no sería posible la sobrevivencia. De los cinco casos tres se presentaron con signos de hipoxia debido a un flujo pulmonar deficiente y dos con insuficiencia cardíaca congestiva. Los del primer grupo se presentaron con cianosis severa a las 24 horas del nacimiento y dificultad respiratoria inmediatamente después. En todos ellos el segundo sonido fue sencillo y sólo uno presentó soplo cardíaco. La radiografía de tórax mostró cardiomegalia en dos y tamaño normal en uno; los tres demostraron prominencia de la curva del ventrículo izquierdo y flujo pulmonar disminuido (Fig. 10). El electrocardiograma que es diagnóstico de esta anomalía mostró eje a la izquierda con hipertrofia ventricular izquierda y agrandamiento de atrio derecho con ondas P melladas (Fig. 11).

Los dos pacientes del segundo grupo con flujo pulmonar aumentado y fallo congestivo se presentaron con dificultad respiratoria y cianosis moderada. El segundo sonido fue sencillo sólo en uno de ellos. Los dos casos presentaron soplo cardíaco. La radiografía de tórax mostró cardiomegalia con patrón de agrandamiento de ventrículo izquierdo y flujo pulmonar aumentado. El electrocardiograma en estos casos mostró hipertrofia biventricular y el eje estaba menos desviado a la izquierda que en los casos del grupo anterior.



Fig. 10: Radiografía de tórax mostrando cardiomegalia con agrandamiento de ventrículo izquierdo y disminución de la vascularidad pulmonar.

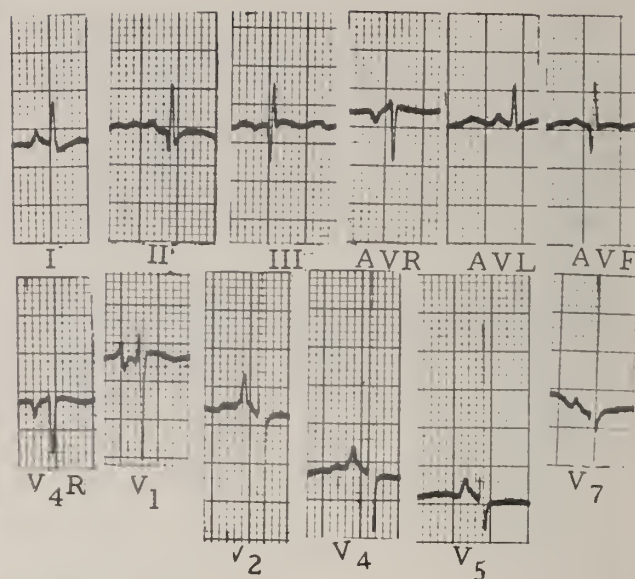


Fig. 11: Electrocardiograma típico de atresia tricuspídea con eje a la izquierda, hipertrofia de ventrículo izquierdo y agrandamiento de atrio derecho.



Fig. 12: Angiograma con inyección en atrio derecho demostrando la secuencia circulatoria en la atresia tricuspídea con defecto interventricular y estenosis pulmonar.



Fig. 13: Angiograma de ventrículo izquierdo demostrando la deformidad en "cuello de cisne" en el tracto de salida del ventrículo izquierdo y la opacificación de las otras tres cámaras cardíacas.

El cateterismo cardíaco permite hacer el diagnóstico con una inyección de contraste en el atrio derecho que opacifica el atrio izquierdo, luego un ventrículo izquierdo grande, siguiendo por un defecto interventricular hacia un ventrículo derecho muy pequeño y llenando una pulmonar pequeña (Fig. 12). Las áreas de obstrucción a la circulación puede estar en el septo interauricular, en el defecto interventricular o en la estenosis pul-

monar.

El tratamiento que hacemos con estos pacientes depende de la variedad a la que pertenecen; cuando la comunicación interatrial no es adecuada se hace una septostomía de balón, como se hizo en dos de nuestros pacientes. En los del flujo pulmonar disminuido se debe realizar una anastomosis sistémico-pulmonar y cuando hay flujo pulmonar aumentado se debe realizar una

constricción quirúrgica de la arteria pulmonar (23).

Canal Atrioventricular Común

Nuestra serie tiene cuatro pacientes con canal atrioventricular común, todos estos se presentaron con insuficiencia cardíaca congestiva, uno presentó además cianosis. Los hallazgos físicos mostraron un soplo de insuficiencia mitral, con un componente pulmonar aumentado y un soplo diastólico en la punta, cardiomegalia severa en la placa de tórax con un flujo muy aumentado. Solo un paciente no mostró en el electrocardiograma el clásico eje desviado a la izquierda que es característico de esta anomalía, todos presentaron agrandamiento de las cavidades derechas. El cateterismo cardíaco demuestra una comunicación libre entre las cuatro cámaras cardíacas. En el angiograma de ventrículo izquierdo se puede apreciar la deformidad de la válvula mitral que es característica (24) (Fig. 13). Cuando no responden al tratamiento con anticongestivos, hay muy poca esperanza en nuestra experiencia de que ellos respondan satisfactoriamente a una constricción quirúrgica de la arteria pulmonar (25).

En la autopsia se ve un orificio central que comunica con todas las cámaras cardíacas debido a una falta en el crecimiento de la porción inferior del septo interatrial, la porción superior del septo interventricular y defectos en ambas válvulas atrioventriculares, todo esto se debe a la deficiencia en la formación de los cojinetes endocárdicos.

Anomalías Cardíacas Complejas

Tres pacientes se presentaron con anomalías cardíacas complejas. Todos tuvieron signos de hipoxia temprana debido a flujo pulmonar disminuido. Dos presentaron soplo cardíaco y en los tres el segundo sonido fue sencillo. Dos pacientes tenían atresia pulmonar y transposición de los grandes vasos. Uno de ellos tenía también ventrículo y atrio comunes, canal atrioventricular completo y dos venas cavas superiores. El otro tenía además dextrocardia, defectos interventriculares e interauriculares. El tercero tenía dextrocardia, cor biloculare y tronco arterioso. Las radiografías de tórax mostraron flujo pulmonar disminuido, el resto de los hallazgos fueron atípicos a excepción de la cianosis que fue constante. En dos de los pacientes se realizó una anastomosis aortopulmonar.

Anomalías Menos Frecuentes

Nuestra serie cuenta con dos casos de tronco arte-

rioso, ambos del tipo 1, (26) en el cual la arteria pulmonar se origina del tronco. Ambos pacientes se presentaron con flujo pulmonar aumentado, fallo cardíaco, soplo y segundo sonido sencillo. La radiografía tenía cardiomegalia y congestión pulmonar. El electrocardiograma demostró hipertrofia biventricular. Uno de ellos tuvo constricción quirúrgica de la arteria pulmonar.

Estenosis pulmonar y atresia pulmonar se presentó en dos pacientes y en otro estenosis aórtica, todos en insuficiencia cardíaca, derecha los primeros e izquierda el último.

Comentarios y Recomendaciones

Hay otras cardiopatías que producen dificultades en el período neonatal y que no están incluidas en el material que se discute, estas son la anomalía de Ebstein, el retorno venoso anómalo total, los anillos vasculares y otras menos frecuentes. También queremos mencionar los defectos que siendo benignos a esta edad, pueden ocasionar problemas en una minoría de pacientes. Estos son: el defecto inter-atrial (27, 28) y el conducto arterioso patente (27).

Las arritmias y las miocarditis pueden producir insuficiencia cardíaca neonatal y finalmente, condiciones extracardíacas como la metahemoglobinemia, la membrana hialina, la fístula traqueo-esofágica, sepsis, poliglobulia, etc., producen manifestaciones muy parecidas a las que se presentan en afecciones cardíacas.

Naturalmente que el diagnóstico precoz empieza en la sala de recién nacidos donde un alto nivel de sospecha por parte de enfermeras y médicos ayudará a reconocerlos; es importante recordar que entre una mitad (29) a dos terceras (27) partes de ellos mueren en la primera semana. Las manifestaciones que surgieron cardiopatía severa son: cianosis, fallo cardíaco, episodios anóxicos y dificultad respiratoria.

Una vez que se admite uno de estos recién nacidos se les hace una evaluación completa con examen físico; radiografía de tórax y electrocardiograma. Si el cardiólogo pediatra cree que el paciente tiene una cardiopatía congénita severa se hacen arreglos para realizar cateterismo cardíaco a la mayor brevedad posible, ya que el paciente puede deteriorarse considerablemente en un par de horas (30).

Generalmente también se notifica al cirujano cardiovascular si se tiene en mente una intervención quirúrgica. Mientras se hacen los arreglos para el cateterismo cardíaco se somete al paciente a una terapéutica médica intensa.

Cuando el diagnóstico está completo se deciden tres tipos de tratamiento que son: 1) Cirugía inmediata

como en la estenosis pulmonar en fallo cardíaco, el retorno venoso anómalo total con obstrucción, etc. 2) Cirugía mediata siempre que el paciente no esté perdiendo terreno y que sea vigilado cuidadosamente aquí estarían comprendidos los cortocircuitos de izquierda a derecha o la coartación de la aorta. 3) Tratamiento médico como en la anomalía de Ebstein o en la insuficiencia pulmonar.

Naturalmente este programa que indicamos es a veces muy difícil de realizar; que junto a la elevada mortalidad tanto médica como quirúrgica lleva en muchas ocasiones a frustraciones y desiluciones pero estas se pueden vencer con inteligencia, experiencia, conocimiento de las facilidades y optimismo.

Resumen

Se hace el estudio de 65 casos comprobados por autopsia de cardiopatías congénitas severas que llevaron a la muerte en las primeras seis semanas de la vida.

Se recalca que aunque el cuadro clínico es muy parecido se pueden apreciar diversas peculiaridades en las diferentes cardiopatías que se describen en orden de frecuencia.

Además de describirse el cuadro clínico, la frecuencia, la patología y el tratamiento, se comenta sobre el catesterismo cardíaco y hacen recomendaciones sobre el manejo de estos enfermos.

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RELACIONES ANATOMICAS ENTRE LA VALVULA PULMONAR Y LA BASE DE LA OREJUELA DERECHA

Renán A. Dieppa, BS
Jorge O. Just Viera, MD

Durante experimentos recientes en los cuales se interpuso un homoinjerto de arteria y válvula pulmonar entre la orejuela derecha y la arteria pulmonar, se pudo apreciar la necesidad de preservar, y quizás aumentar el volumen atrial. Al cerrarse quirúrgicamente la válvula tricúspide en un intento de simular atresia de esta válvula, el atrio derecho se constituye en el depósito intracardiaco para admitir el retorno venoso sistémico y propulsarlo a los pulmones a través del puente atriopulmonar.

Consideramos importante estudiar la relación entre la válvula pulmonar y la base de la orejuela derecha, porque al suturar a la orejuela el anillo valvular del homoinjerto de arteria pulmonar obtenido de otro animal de peso y tamaño similar al recipiente, bien podría resultar en una estenosis parcial funcional e impedir el retorno venoso sistémico.

Materiales, Métodos y Resultados

Se obtuvieron los corazones de seis perros. Después de pesarlos y disecarlos, la válvula pulmonar se midió en dos niveles, a nivel del anillo valvular y a un centímetro de distancia de éste. Amputada la orejuela derecha, se midió la circunferencia de la base, a 0.5 cm. y a 1.0 cm. de la punta de la orejuela. Pudo determinarse la razón entre todas estas medidas, las de la válvula pulmonar y las de la orejuela, y entre ellas mismas (Tabla I).

En las medidas obtenidas, existe una razón ascendente, de 1 a 2 a 4 entre las medidas de la circunferencia de la orejuela, a niveles de 0.5 cm., 1.0 cm. y la base, respectivamente. El anillo de la válvula pulmonar tiene una circunferencia un poco mayor que la base de la orejuela, sin embargo, el diámetro de la arteria pulmonar disminuye progresivamente y a 1.0 cm del anillo, es menor que la circunferencia de la base de la orejuela derecha.

Discusión

Nos propusimos, al llevar a cabo este limitado estudio, determinar la mejor manera de obtener un homoinjerto de arteria y válvula pulmonar propicio para un puente atriopulmonar. Revisar la literatura fue actividad yerma, pues no hay información publicada sobre este tema.

Determinamos cierta diferencia en tamaño que bien puede resultar en una posible estenosis funcional debido a las relaciones anatómicas entre el diámetro de la válvula pulmonar y la base de la orejuela derecha, si se usan animales de igual tamaño y peso. Esta diferencia en tamaño, junto a la superficie irregular, tosca y trabeculada de la orejuela, puede predisponer a trombosis en anastomosis construídas entre la base de la orejuela derecha y el anillo valvular de la arteria pulmonar. Además, la sutura constrictiva de la anastomosis magnificará la tendencia a trombosis al disminuir aún más el diámetro efectivo del anillo valvular pulmonar.

Este problema puede obviarse al usar homoinjertos obtenidos de donantes de mayor tamaño que el recipiente; ciertamente esto es posible en humanos al obtenerse válvulas y arterias pulmonares de cadáveres adultos jóvenes para su uso en niños. Otro método, inaugurado en algunos experimentos subsiguientes, es suturar un pedazo de pericardio al anillo de la válvula pulmonar de tal manera que aumente el volumen del atrio derecho y la circunferencia de la base de la orejuela.

Estas consideraciones adquieren toda su importancia cuando se comprende que se tratará de resultados a largo plazo en niños, afectados por el crecimiento.

Resumen

Se midió en perros la circunferencia del anillo de la válvula pulmonar y a 1.0 cm del anillo; de la base de la orejuela y a 0.5 cm y 1.0 cm de la punta de la orejuela. La razón entre estas medidas fue ascendente para la orejuela y descendente para la arteria pulmonar. La circunferencia del anillo de la válvula pulmonar es un po-

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TABLA I: MEDIDA DE LAS CIRCUNFERENCIAS DE LA BASE DE LA OREJUELA DERECHA Y DEL ANILLO DE LA VALVULA PULMONAR, A 0.5 CM. Y 1.0 CM. DE LA PUNTA DE LA OREJUELA Y A 1.0 CM DEL ANILLO VALVULAR

No.	Peso Animal	Peso Corazón	Orejuela Derecha			Válvula Pulmonar	
			Base	0.5 cm.	1.0 cm.	Anillo	1.0 cm.
1	19 lbs.	69 gms	---	0.9 cms	1.8 cms	4.0 cms	2.6 cms
2	25 lbs.	87 gms	5.0 cms	1.0 cms	1.8 cms	5.3 cms	3.5 cms
3	30 lbs.	104 gms	7.0 cms	1.9 cms	3.6 cms	4.8 cms	2.6 cms
4	25 lbs.	86 gms	3.9 cms	0.9 cms	2.0 cms	4.2 cms	2.6 cms
5	30 lbs.	132 gms	4.8 cms	1.7 cms	2.8 cms	6.0 cms	4.1 cms
6	18 lbs.	108 gms	3.9 cms	0.9 cms	2.0 cms	4.2 cms	2.8 cms

co mayor que la circunferencia de la base de la orejuela. Se discute la importancia de estas relaciones anatómicas en selección del tamaño de un homoinjerto para la construcción de un puente atriopulmonar.

Summary

Measurements of the circumference of the pulmonary

valve and the pulmonary artery at 1.0 cm from the valve compared to measurements of the circumference at the base of the right auricle and at 0.5 cm and 1.0 cm from the base. The importance of the relationship between such measurements in patency of an anastomosis between a pulmonary homograft and the base of the auricle is discussed.

HEXACLOROFENO

Desde diciembre de 1971 en que la Administración de Drogas y Alimentos de los Estados Unidos llamó la atención sobre la toxicidad del hexaclorofeno y prohibió su uso indiscriminado, las controversias sobre el particular han ido en aumento. Un mes más tarde el Comité del Feto y del Recién Nacido de la Academia de Pediatría envió un comunicado donde expresa lo siguiente:

"Los riesgos en el uso de las sustancias que contienen hexaclorofeno para el baño diario de recién nacidos aún no se ha establecido. Se han encontrado bebés con niveles en sangre que se acercan a los niveles tóxicos experimentales. Por consiguiente, el uso del hexaclorofeno para el baño de los recién nacidos bien sea en los hospitales como en el hogar está contraindicado."

El hexaclorofeno es un agente antibacteriano que se le añade a algunas soluciones sépticas, a jabones y cosméticos. Se absorbe por piel normal. La rapidez de absorción, su metabolismo y su forma de eliminación en el ser humano aún se desconocen. Se ha encontrado que a niveles tóxicos en ratas produce edema cerebral y vacuolización generalizada de la corteza cerebral. En los seres humanos la toxicidad se manifiesta por irritabilidad del sistema nervioso central y puede llegar hasta convulsiones.

Su uso se generalizó en las salas de recién nacidos donde se requería una solución al 3 por ciento para bañar a todos los bebés. Coincidentalmente con el uso rutinario de este agente se observó una disminución dramática en la incidencia de infecciones estafilocócicas en las salas de los recién nacidos. Ignoramos cuál fue la participación de este agente en este tipo de infecciones. ¿Qué ocurrirá ahora en las salas de los recién nacidos con la incidencia de infecciones estafilocócicas? No lo sabemos. Debemos recordar que nuestros conocimientos sobre asepsia han mejorado progresivamente. Han comenzado a aparecer casos de bebés recién nacidos con infecciones estafilocócicas nuevamente; pero aún es temprano para decir a ciencia cierta si hay una correlación directa o no con la falta de uso del hexaclorofeno.

Hasta tanto no se lleven a cabo estudios controlados sobre el particular, su uso rutinario por el público y en los recién nacidos está contraindicado. En otros pacientes, si su uso es necesario se deben instruir tanto al paciente como a los familiares que el área que se ha impregnado con el hexaclorofeno se le debe hacer un enjuague minucioso con agua clara. Igualmente se les debe informar la toxicología y como ésta se manifiesta.

Mercedes Vega-Vidal, MD
Presidente
Sección Pediatría AMPR

NOTA: Posterior al envío de este editorial a la Junta Editora de este Boletín hubo una reunión en las oficinas centrales en Washington de la Administración de Drogas y Alimentos con representantes del Center for Disease Control (CDC), del Comité del Feto y del Recién Nacido de la Academia de Pediatría y el Presidente de Comités de la Academia de Pediatría, éste último en representación de la directiva de la Academia. Las recomendaciones finales no fueron alteradas excepto por lo siguiente:

"Si ocurriese un brote de infecciones estafilocócicas en una sala de recién nacidos se deben re-evaluar las facilidades físicas y técnicas existentes y si éstas se consideran inadecuadas, corregirlas inmediatamente. El uso de hexaclorofeno al 3 por ciento seguido de enjuagues con agua clara debe ser considerado como parte del programa para controlar las infecciones estafilocócicas. Su uso debe ser a corto plazo y sólo una vez al día. Bajo ninguna circunstancia el uso del hexaclorofeno para bañar bebés en las salas de los recién nacidos debe ser el sustituto de servicios de calidad óptimos en los hospitales".

Mercedes Vega Vidal, MD

OBSOLETE EXCUSES OR OBSOLETE FACILITIES?

In a recent editorial Dr. Just Viera congratulated the pediatric cardiology section at the University of Puerto Rico Hospital for helping to bring the management of congenital heart disease to its present state of development in Puerto Rico (1). I concur in the congratulations and admire the magnificent display of devotion and determination by the pediatric cardiologists, in improving the care of children with congenital heart defects in Puerto Rico. I would include in my congratulations the cardiovascular surgeons who participated in those efforts, since the successful management of congenital heart disease depends on intimate cooperation between pediatric cardiologists and cardiovascular surgeons, as demonstrated by the three papers published in the February, 1972, issue of *Boletín*.

Social justice demands that there not be a "double standard" in health care of any type (1). The aim in Puerto Rico should be to establish one cardiac center where adequate facilities would be available to manage all children with congenital heart disease, whether they are indigent or paying patients. Previous experiences have shown that the best results are obtained in a cardiac referral center, where highly specialized facilities as well as personnel are available 24 hours a day (2). The fact is that such a center is presently not available in Puerto Rico. It is a tribute to the competence of the pediatric cardiologists and cardiovascular surgeons at the University Hospital that they have accomplished so much with suboptimal facilities. Their outpatient clinics are overcrowded, they have difficulty obtaining space to admit patients who require hospitalization, and they still lack an adequate pediatric cardiac catheterization laboratory. The pediatric cardiologists are forced to use, when available, a catheterization laboratory that does not have such necessary equipment for the study of congenital heart disease, as a biplane seriograph or a videotape recorder.

The physician who refers a patient with a serious illness like congenital heart disease, to a referral center, has the professional responsibility to refer him to the best possible center available to that individual patient. It is unfair to suggest that physicians and charitable organizations are derelict in their obligation to support the Puerto Rican effort, when they refer children with cardiac defects to centers outside Puerto Rico (1). They are aware of the competence of pediatric cardiologists and cardiovascular surgeons in Puerto Rico, but they are also painfully aware of the limited facilities presently available.

In the United States, one out of every one hundred children is born with a congenital heart defect (2). Fifty percent of them die within the first year of life unless adequate diagnostic and treatment facilities are available. The figures for Puerto Rico are probably similar. The entire Puerto Rican community, including public and private agencies, needs to accept its responsibility to provide an adequate center to meet this important health problem within Puerto Rico. Until then, it is unfair to condemn individual patients and their physicians for seeking help elsewhere.

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NOTA DEL EDITOR:

Nuestro editor invitado levanta nuevamente la necesi-

dad de proporcionar facilidades adecuadas para pacientes con lesiones cardíacas congénitas. Para todas las lesiones cardíacas, cabe añadir.

Repaso del editorial aludido "Ejemplo, problemas y preguntas" revela que logró su propósito de crear conciencia sobre este problema hasta ahora afrontado solitariamente por nuestros cardiólogos pediatras. En ningún momento se "condena" al paciente que busca su salud en otras tierras, ni al médico que allí lo refiere.

Sí se señala vigorosamente que "todavía evaden sus responsabilidades al enviar fuera de su país pacientes pediátricos con lesiones congénitas!" Responsabilidad bien subrayada por el Dr. Rodríguez-Fernández: crear aquí las facilidades necesarias. Vamos más lejos. Cada paciente en necesidad de buscar tratamiento adecuado fuera de Puerto Rico es testigo vivo de la incapacidad nuestra en establecer las facilidades necesarias. De seguir la vía de menor resistencia, para cumplir con nuestra "responsabilidad profesional" habría que referir a Es-

tados Unidos a un buen segmento de la población, incluyendo aquéllos en Culebra sin acceso a cuidado médico. Ahí está el detalle: tenemos una ineludible responsabilidad personal y social que cumplir. Quienes van a Centros Médicos del exterior tienen los medios para sufragar los gastos, pero, ¿y los demás? Huérfanos de tratamiento, ajenos a la posibilidad de cura posible, sufren calladamente el curso natural de su enfermedad.

Jorge O. Just Viera, MD

ARTICULOS APROBADOS POR LA JUNTA EDITORA
PARA PUBLICACION EN EL BOLETIN MEDICO DE LA
ASOCIACION MEDICA DE PUERTO RICO

1. Multiple Sclerosis in Puerto Rico (Experience at the University Hospital) I. Review of a Series of Cases
L. P. Sánchez Longo, MD, Miguel Fiol, MS IV and Pedro Cedó, MS IV
2. Programa Médico Regional de Diabetes - Objetivos, Logros y Proyecciones
Lillian Haddock, MD, FACP
3. Treatment of Drug Resistant Hypertension in Chronic Kidney Disease
José L. Cangiano, MD, Rafael Ramírez González, MD, Osvaldo Ramírez Muxó, MD, Enrique Pijem, MD and Elaine Waddell, BS
4. Semblanza del Dr. Ramón J. Sifre — El Tratamiento de las Complicaciones de la Cirrosis Hepática Avanzada
A. Fernós Isern, MD
5. The Dextrocardias — A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects
Charles D. Johnson, MD

NOTICIAS

THE 10TH ANNUAL CANCER CHEMOTHERAPY CONFERENCE will be held at the University of Wisconsin, Madison, on September 6-8. The program will include a review and forward look at anti-cancer therapy, multiple drug therapy of solid tumors and leukemias, the role of x-ray therapy, immunology and virology in the treatment of cancer. For information contact Dr. G. Ramírez, 714C University Hospitals, Madison, Wisconsin, 53706.

JAMA CALLS FOR DELAY IN TEST-TUBE BABY IMPLANTS

CHICAGO— A moratorium should be declared on any further experiments to implant a "test-tube baby" into a woman's womb, an editorial urged today in the current (May 1) issue of the *Journal of the American Medical Association*.

Representatives of various disciplines should assemble to discuss the ethical considerations of such procedures as the growth and implantation of fertilized eggs outside the body (the "test-tube baby") and cloning, an asexual method of reproduction that would produce children genetically identical to their parent, the editorial urged.

The matter is particularly urgent since fertilized eggs have already been grown outside the body and some researchers are talking about implanting these "test-tube babies" in humans on a trial-and-error basis. This would make it possible for a woman otherwise unable to conceive to become a mother.

HEROIN USE DIFFERS IN VIETNAM, U. S.

CHICAGO — The pattern of heroin use by American soldiers in Vietnam differs significantly from heroin use in the United States, a Massachusetts physician reported in the current (May) issue of *Archives of General Psychiatry*, a publication of the American Medical Association.

Norman E. Zinberg, M. D., said that the most important difference was that users in Vietnam took heroin primarily as a social gesture and were usually members of small heroin-taking groups who were disillusioned with the "non-war" and the Army. In contrast, users in the U. S. were usually "loners". Dr. Zinberg made his observations after interviewing hundreds of Army personnel during a three-week survey of heroin use

and user rehabilitation efforts in Vietnam.

Other differences noted were:

Users in Vietnam were of many personality types and backgrounds and most had little previous drug experience. U. S. users had heavy previous drug experience, often showed character disorders and came from a big city with a middle class or ghetto background.

Heroin in Vietnam was strong and easy to get. It was smoked, snorted, or swallowed; until recently mainlining (intravenous injection) was rare. Heroin in the U. S. is hard to get, expensive, and is mainlined exclusively.

THE HEXACHLOROPHENE STORY (Abstract) By Wayne L. Pines, Office of the Assistant Commissioner for Public Affairs, Food and Drug Administration

The Food and Drug Administration's regulatory action to restrict the use of hexachlorophene was based mainly on three studies, reported in the past several months and concurred in by scientific experts, challenging the safety of the widely-used antibacterial drug.

The studies led to an FDA reappraisal of hexachlorophene to determine whether the benefits of its use in a large number of products and in hospital nurseries outweighed the risks to the public and especially to newborn infants. FDA concluded that hexachlorophene, when used incorrectly or indiscriminately, poses a potential hazard to both adults and children, and therefore should be restricted.

Story Starts in 1941

The hexachlorophene story began in 1941, when W. S. Gump patented it. A Swiss-based company, Givaudan Corporation, developed it. Hexachlorophene's use grew and grew over the years. It has been an ingredient in creams, ointments, powders, cosmetics, toothpastes, antiperspirants, mouthwashes, feminine deodorant sprays. It has been used widely to treat burns and for daily cosmetic uses such as showering and skin care. Hexachlorophene has even been used in furnace filters and in plastics for shower curtains.

Hexachlorophene has been popular for a number of reasons. Everyone assumed its medical action was well-known and well-understood. It is a relatively insoluble chemical, which may have led to the belief that it could not be very potent. And FDA itself for some years did not regard products containing hexachlorophene to pose a hazard to the public.

The Three Studies

Random observations and limited studies of hexachloro-

phene were all that was available until August 1971, when the first of three studies leading to the recent regulatory restrictions was published. This study was performed by Dr. Renate Kimbrough and Thomas Gaines, two scientists then working in FDA who were considering an application by a manufacturer who wanted to use hexachlorophene as an herbicide. Kimbrough and Gaines fed hexachlorophene to rats as part of their diet. After two weeks, the rats developed leg weakness which progressed in three to five weeks to paralysis. After hexachlorophene was discontinued, the rats regained use of their legs—indicating that whatever damage is caused by hexachlorophene may be reversible.

Kimbrough and Gaines also found, however, that the brains of the hexachlorophene-fed rats were heavier than those of the rats in the control group. Lesions (abnormal spaces) were observed in the brains of the hexachlorophene-fed rats. The scientists concluded that indiscriminate and unnecessary use of hexachlorophene should be discouraged.

Dr. Kimbrough, now with the Environmental Protection Agency, took a broader look at hexachlorophene in another article published in August 1971. She undertook a thorough review of the scientific literature to collate what already was known about the chemical. She pointed out that hexachlorophene is absorbed through normal skin and that large doses of the chemical affect the central nervous systems of both humans and rats. Again, she urged that unnecessary use of hexachlorophene be discouraged.

The second study leading to the FDA regulatory restrictions related hexachlorophene to human babies. This study was reported by a team of scientists, including August Curley, Robert Hawk, and Dr. Kimbrough. It involved 50 newborn infants in a New York hospital who were washed once daily with a diluted hexachlorophene solution according to established hospital practice. None of the infants showed any toxic effects—but the investigators found the babies had absorbed hexachlorophene into their bloodstreams through normal, unbroken skin, and that the levels were close to the toxic levels in animals and man.

The third study was received by FDA in November 1971 from Sterling Drug, Inc., the manufacturer of the most widely used 3 percent hexachlorophene solution, pHisoHex. The study involved five newborn monkeys washed daily for five minutes with pHisoHex for three months in a manner simulating the washing of newborn infants. The monkeys showed no overt signs of adverse reactions—but autopsies revealed that the monkeys' brains had lesions similar to those observed in the brains of the rats that had been fed hexachlorophene. Monkeys washed similarly without hexachlorophene were normal.

Hexachlorophene in General Use

While the controversy over hexachlorophene use in newborns was bubbling, FDA turned to the broader question of hexachlorophene for general use. In considering this problem, FDA scientists applied a second concept in addition to benefit versus risk:

Even if hexachlorophene could be used safely in any single product, its mode of use had become such that a consumer could be exposed to large amounts of the antibacterial agent from a variety of sources during one day. The "total body burden" of hexachlorophene could become dangerously high. If a woman, for example, used a toothpaste, mouthwash, deodorant, powder, cream and feminine spray containing hexachlorophene—

a possibility that was not unreasonable—she could develop dangerous blood levels of the chemical.

Could a Federal regulatory agency, responsible for protecting the American consumer from avoidable hazards, permit the continued marketing of such a large number of products that contained hexachlorophene? The answer reached by Agency scientists and policymakers was that some regulatory action was needed. Hexachlorophene had become an environmental contaminant in that millions of Americans carried traces of the chemical in their bloodstreams. The potential for harm was too great.

FDA proposed to limit the least important use of hexachlorophene in products that could be purchased by consumers in supermarkets and pharmacies, without preventing its most important use for medical purposes. The Agency divided hexachlorophene-containing products into three categories: drugs with small amounts of hexachlorophene; drugs with higher concentrations such as those used to bathe newborns in hospitals; and cosmetics.

For drugs containing small amounts of hexachlorophene, such as soaps advertised for deodorant use, FDA proposed that they should be marketed only with the Agency's approval. The labels of these products should contain the warning: "Caution: Contains Hexachlorophene. For external washing only. Rinse thoroughly." The purpose of this policy was to make sure that hexachlorophene is used appropriately in drugs, soaps, and other consumer products, and that consumers are advised to rinse thoroughly, lest the chemical remain on the skin and possibly enter the bloodstream.

FDA proposed that drugs with higher concentrations of hexachlorophene—that is, any product containing more than .75 percent—should be placed on a prescription basis. This would restrict their uses to situations in which they are medically necessary, as determined by a physician. FDA made clear, however, that this would in no way restrict the use of high concentrates such as pHisoHex as surgical scrubs or disinfectants in hospitals or in physicians' and dentists' offices. In fact, the Agency again advised physicians and nurses to continue to wash their hands in 3 percent hexachlorophene solutions. FDA's reasoning was that the benefits of restricting the spread of bacteria in hospitals and in physicians' offices outweighed the risk of absorbing hexachlorophene from hand washing.

But the scientific evidence clearly dictates the need for restrictions on hexachlorophene to protect the American consumer. FDA believes that it has no choice but to take the action it has proposed—particularly because hexachlorophene is so widely and indiscriminately used and is thought to be safe. It is clear, however, that its effects are not always evident to the naked eye but can adversely affect body chemistry and mechanisms.

It's difficult to change, but when new evidence comes along that indicates that some products may create an unwarranted hazard, then change is necessary. In the case of hexachlorophene, change in patterns of use is clearly dictated. The three studies that provided the basis for FDA's action all lead to the conclusion that unrestricted use of the chemical in consumer products and in hospital nurseries poses a potential hazard.

The hexachlorophene story is not black-and-white. As with all medications, there are real benefits to be accrued from the use of this antibacterial, but there are some real risks as well.

Additional research is needed before the hexachlorophene story can be written in final form.

FDA recognizes the value of hexachlorophene as an anti-bacterial drug. The restrictions are designed to make sure that hexachlorophene is used appropriately and safely to protect the

American consumer. FDA has initiated those restrictions in the name of the consumer, for safety's sake.

(Preprint from FDA Papers — April 1972)

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BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

THE DEXTROCARDIAS. (FIRST PART)

A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects. 165

Charles D. Johnson, MD

MULTIPLE SCLEROSIS IN PUERTO RICO (EXPERIENCE AT THE UNIVERSITY HOSPITAL)

I. Review of a Series of Cases..... 176

L. P. Sánchez Longo, MD, Miguel Fiol, MS IV and Pedro Cedó, MS IV

MANAGEMENT OF ACUTE SCROTAL SWELLING IN CHILDREN AND YOUNG ADULTS 179

Roberto F. Fortuño, MD

**LEY NUM. 22 – LEY QUE REGULA LA
PRACTICA DE LA MEDICINA EN PUERTO RICO 183**

CARTAS A LA REDACCION 190

NOTICIAS 193



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in congestive heart failure...

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six.

Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

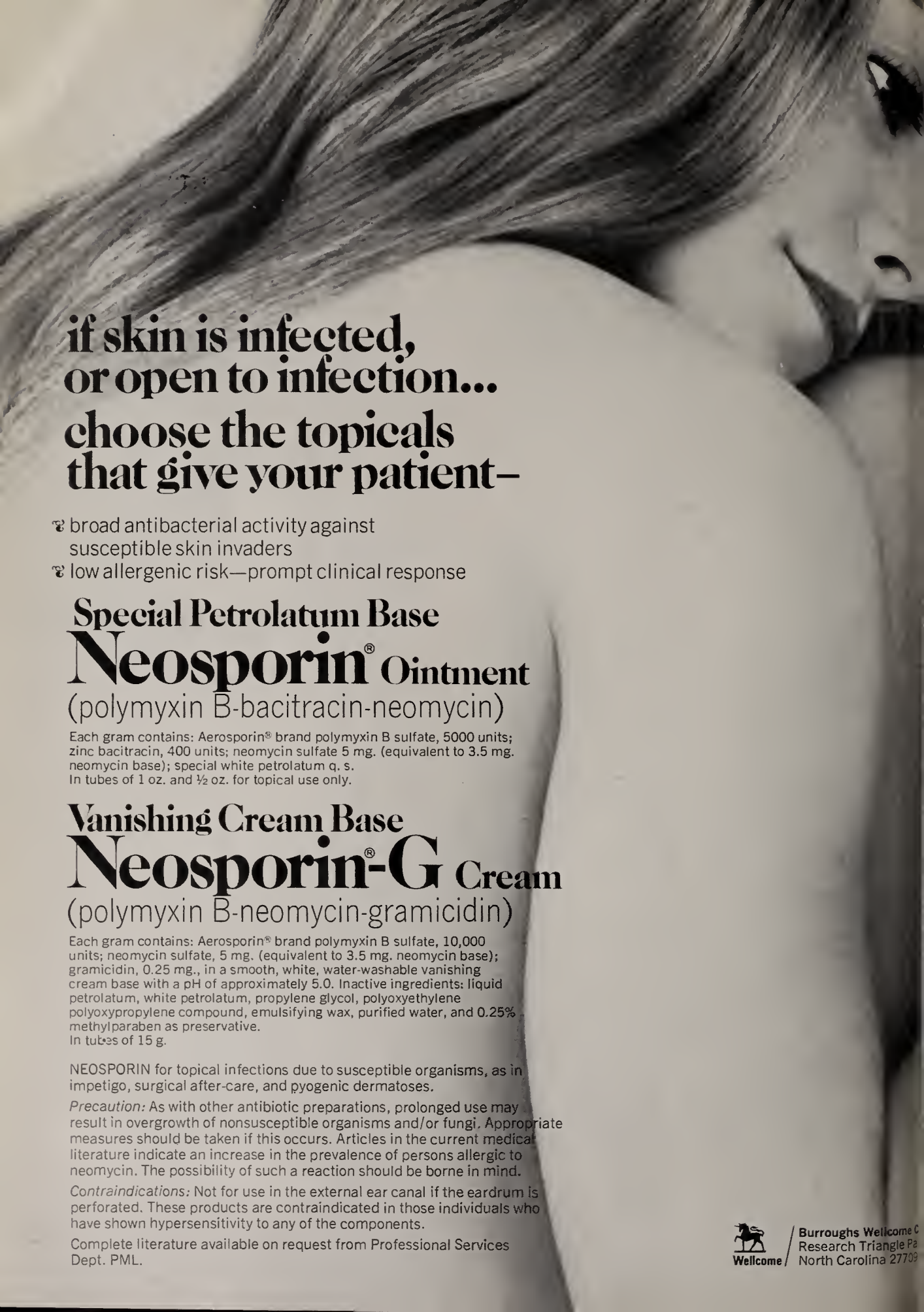
Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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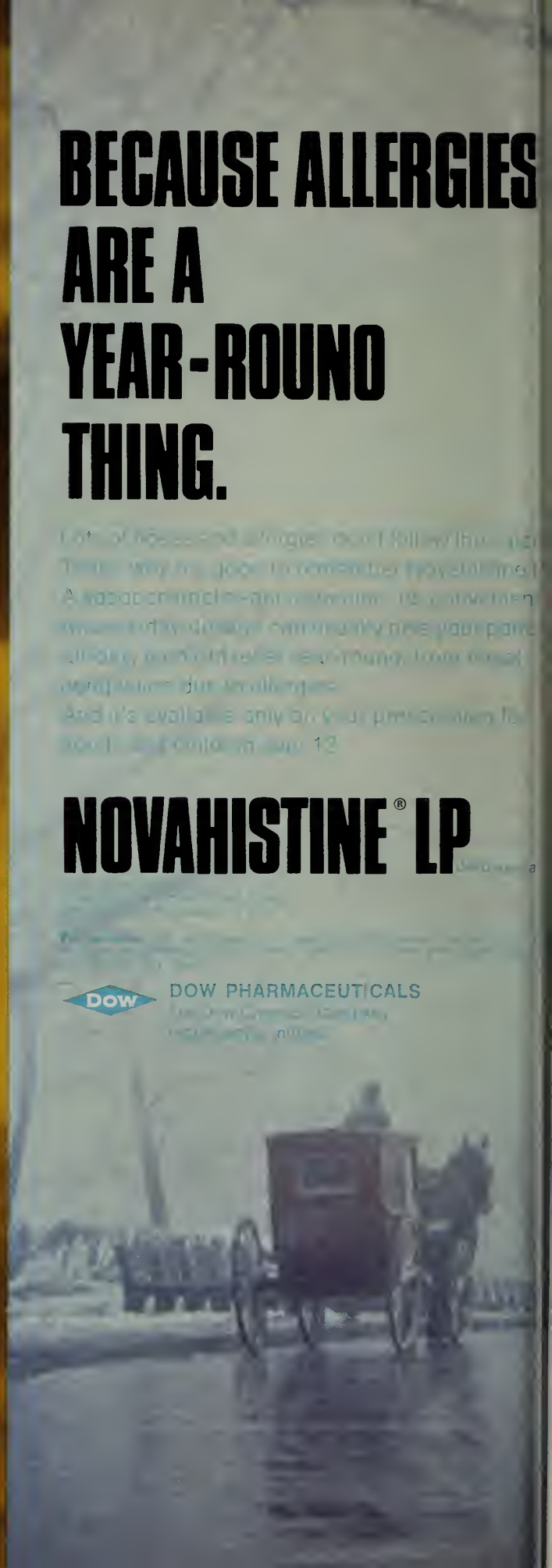
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THE DEXTROCARDIAS. *A Review and a Report of 26 Cases, Emphasizing Electrocardiographic & Vectorcardiographic Aspects.* (FIRST PART)

Charles D. Johnson, MD

Dextrocardia, right-sided hearts, has captured the interest and enthusiasm of physicians since ancient times. Aristotle observed visceral inversion in animals more than 300 years B. C.; dextrocardia was described for the first time by Fabricius in 1606, and dextrocardia with situs inversus was identified in 1643 by Severinus of Rome. Riolanus in the 17th century reported 2 cases, one of whom was Queen Marie de Medici. The electrocardiographic findings in dextrocardia with situs inversus totalis were first presented by Waller in 1889 (1).

The incidence of dextrocardia is not known but has been stated to be about 1 case per 9000 persons. This would suggest that there are about 311 cases of this anomaly in Puerto Rico. Three–5 percent of individuals with congenital heart disease have dextrocardia.

The medical literature on the dextrocardias and the cardiac malpositions (including transpositions of the great vessels, atrial and ventricular inversions, which are sometimes associated findings) is complicated and rendered difficult by the numerous and complex classifications. Some of the more recently proposed classifications are those of Campbell (2), Lev (3, 4), Rosenbaum (5), Arcilla and Gasul (6, 7), Friedberg (8), Elliott (9, 10), Shaher (11), Stanger and Edwards (12), the Van Praaghs (1, 13), Miller and Sodi-Pallares (14), and Davis and Pryor (15). The classification of the Van Praaghs', in the opinion of the author, appears to be the most accurate and rational. This classification is based upon an embryological and anatomical framework, emphasizing anatomical features and associated anomalies, while de-emphasizing the actual location of the heart and cardiac apex (such as dextrocardia, mesocardia, levocardia, etc.), the use of a physiological terminology (such as "venous" and "arterial" ventricles), and the use of such terms as "mirror-image dextrocardia, dextroversion, dextrorotation, pivotal dextrocardia, dextroposition and corrected transposition.

However, the classifications of Lev (3, 4), Arcilla and Gasul (6, 7), and Miller, Medrano and Sodi-Pallares (14), are relatively simple and lend themselves well to electrocardiographic and vectorcardiographic use. So, these classifications will be used in this report, correlating them later to some extent with the Van Praagh and other nomenclatures.

Classification

- I "Mirror-image" Dextrocardia
 - A. Without Cardiopathy
 - B. With Cardiopathy
 - 1. Acquired
 - 2. Congenital
- II Dextroversion
- III Mixed Dextrocardias
 - A. With Atrial Inversion
 - B. With Ventricular Inversion
- IV Indeterminate Situs
- V Dextroposition
- VI Technical "Dextrocardia"
- VII Levoverversion

Much has been written on the electrocardiographic features of dextrocardia, but vectorcardiographic reports are few. A recent excellent vectorcardiographic study is that of Miller, Medrano and Sodi-Pallares (14), which comprised 20 vectorcardiograms from 17 patients. These were obtained by the cube (Grishman) system of electrode placement; inverted cube loops were also obtained. The present study utilized the Frank system of electrode placement, a corrected orthogonal system, which is probably the most popular clinically used system at the present time. Electrocardiograms were also studied.

Figure 1 shows diagrams of the positions of the cardiac chambers, great arteries, venae cavae, and abdominal viscerae in the normal heart, various types of dextrocardia and levoverversion.

Materials and Methods

From the University Hospital, UPR Medical School, Cardiology Section, Río Piedras, P. R. 00935

This report consists of an electrocardiographic and vectorcardiographic study of 25 patients with some form of dextro-

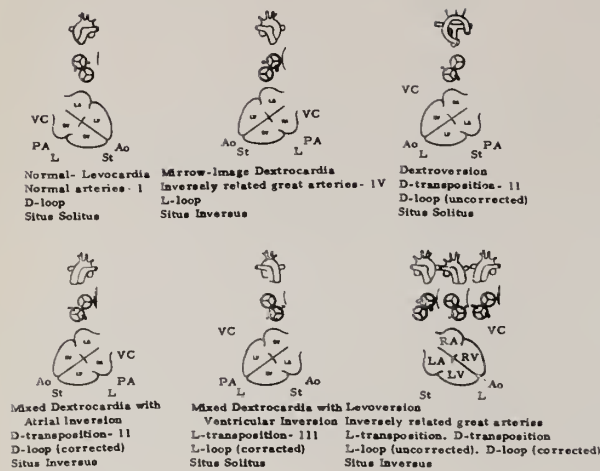


Fig. 1: Diagrams of the positions of the cardiac chambers, great arteries, venae cavae and abdominal viscera in the normal heart, various types of dextrocardia and in levoversion. RA-morphologic right atrium; RV-morphologic right ventricle; LA-morphologic left atrium; LV-morphologic left ventricle. (After Van Praagh and Vlad¹, Lev et al⁴, and Cleland et al⁴⁶).

cardia, and 1 patient with levoversion. In addition to the electrocardiographic and vectorcardiographic analysis, a review of the patients' clinical records, roentgenographic reports, cardiac catheterization data and angiograms, and autopsy data, when available, was also made. The electrocardiographic analysis consisted of a description of the P wave configuration and axis, the PR interval, the QRS and T morphologies in particular leads, and the heart rate. Any arrhythmia was characterized. In some of the patients, right precordial leads were available for study. The vectorcardiographic analysis consisted of several parameters: the rotation and location of the P and T loops, a description of the rotation, major location of the QRS loops, and maximum QRS vector location (degrees) in the horizontal (H), right sagittal (RS) and frontal (F) planes. The 0.01 and 0.02 second and "late" vectors were noted in the H. plane, (this can involve some difficulty if the initial or late vectors are obscured at the E point). The orthogonal leads X, Y and Z were described.

An attempt was made for specific anatomical location and characterization of the heart, including the atria and ventricles (non-inversion, inversion), and the great vessels (non-transposed, transposition). However, even after using all methods of diagnosis, including angiography for anatomical ventricular identification, complete accuracy and identification may be less than desirable.

The vectorcardiograms (VCG) were performed using a Sanborn (H-P) VCG instrument (Viso Scope 780-6A and programmer 1507 A) and the loops were photographed with a Polaroid camera, using number 107 Polaroid film. The Frank system of electrode placement was followed. At X1 magnification, 1 cm. equals 0.5 mv; X0.5 means 2 x magnification and X0.2 means 5 x magnification. A calibration has been photographed in most of the studies. Each tear drop equals 2.5

milliseconds (msec) (4 tear drops = 10 msec. = 0.01 second). The blunt part of the tear drop leads.

Results

Of the total group of 26 patients, 16 were classified as "mirror-image" dextrocardias; 10 of those were without cardiopathy, simple mirror-image dextrocardia; 6 were associated with cardiopathy, 2 of an acquired type (left ventricular hypertrophy), and 4 complicated by congenital heart lesions. Three patients were included in the dextroversion group, and 4 patients in the mixed dextrocardia group, 3 with atrial inversion, and 1 with ventricular inversion. One patient was in the indeterminate category, and one case with "technical dextrocardia" was included. One patient with the rare anomaly of levoversion was included. Most patients had both an electrocardiographic and vectorcardiographic study; in others only an electrocardiogram (ECG) was available.

Table I is a diagnostic table including classification, age and sex, pertinent clinical data, anatomical diagnoses, diagnostic basis, and anatomical diagrams (boxes).

The ages of the patients ranged from 1 month to 85 years, all but 2 of the patients being in the adult age group. Sixteen of the patients were females and 10 males. Autopsy data was available in three cases.

I. Mirror-Image Dextrocardia.

A. Without Cardiopathy. (Figures 2 and 3)

The electrocardiogram (ECG) in these 10 cases revealed the typical pattern previously noted in simple, uncomplicated mirror-image dextrocardia. The vectorcardiogram (VCG) showed the QRS and T loops to be located to the right, with clockwise QRS rotation in the H and RS planes and either clockwise or counterclockwise rotation in the F plane. The P loops were located to the right and rotated variably. The H and F planes demonstrate this change from the situs solitus heart, while the sagittal plane shows no significant change. The maximal QRS vectors in the H and F planes averaged 180° and 155° respectively. In two cases the I, A and C electrodes were inverted, changing the QRS loops to the left, posteriorly and inferiorly (case 4 and case 10); in Case 10 the maximal H plane vector changed from +173° to -3° and -88°, while the maximal F plane vector changed from +158° to +20°. Interchanging the right and left arm lead wires "normalized" the ECG.

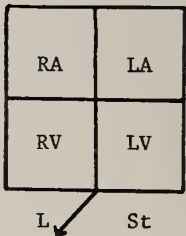
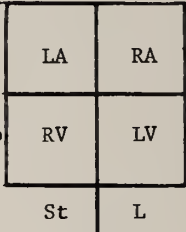
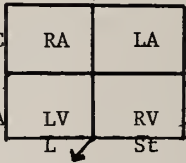
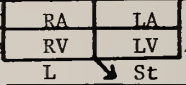
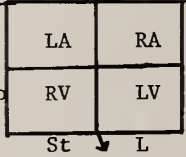
B. With Acquired Cardiopathy.

Two patients were included in this group; one patient with left ventricular hypertrophy (LVH) (Case 2)

TABLE I: DIAGNOSES

Group	Case No.	Age & Sex (Years)	Associated Conditions	Diagnostic Basis	Boxes
<i>I. Mirrow-Image Dextrocardia</i>					
Without Cardiopathy	1	16 F	Systolic murmur. H. of goiter, hypothyroidism.	Clin. X-ray ECG	
	2	14 M	RBC's in urine. Back pain. ? Aorta on left. Testicles same level app.	"	
	3	20 F	Gr. 11 systolic murmur. ? ARF.	"	
	4	15 M	Kartagener's Syndrome	"	
	5	65 F	Bronchial asthma. FH Chronic bronchitis. Sinusitis. Hypertension. Chronic cholecystitis.	Abdominal surgery.	
	6	52 F	Bronchial asthma. ? ASHD. Systolic murmur. Exotropia. H. of hypertension.	"	
	7	53 F	Bronchial asthma. Frontal sinus hypoplastic. Hypertro- phy of nasal turbinates; probably polyp maxillary sinus.	"	
	8	35 F	Pre-eclampsia. Cases 5, 6 and 7 are her aunts.	Clin. ECG	
	9	38 F	Pregnant. Possible VSD.Card.	"	
	10	24 F	Uterine fibroma. Tubal occlusion.	"	
With Acquired Cardiopathy.LVH.	11	67 F	HCVD, ASHD(? diaphragmatic MI). CVA. Fibrotic changes at lung apex.	"	
	12	76 M	Trauma-auto accident. Septicemia. Pneumonia.	"	
With Congenital Cardiopathy	13	60 M	ASD. Af. VT. High-grade AV block. Pacemaker, CHF. Chronic maxillary inflamm- atory disease. Agenesis of frontal sinuses. Pericarditis.	Cath Angios Autopsy	
	14	32 M	TF vs. DORV,etc. L to R shunt. R to L shunt.Cyanotic.LVH. Gout. Hb.-22.4 gms.VSD.PS. Inguinal hernia; varicocele. Bifid rib. Osteoma of frontal.R-H. sinus.Anomalous maxillary sinus.	" Ao Cath(inc) Angios	
	15	22 M	"TF", valvular PS. Left aorta and innominate artery.Murmur. Cyanotic.Hb.-22.8 gms.Brock operation in 1961. Decreased air content in sinuses. R-H. Breasts in low 3 rd IS. Inguinal hernia.Right testicle lower or same level.	" Cath Angios	
	16	22 M	Taussig-Bing Anomaly vs. DORV vs. TF. CVA.	" Cath(inc) Angios	

TABLE I: DIAGNOSES (Cont.)

Group	Case No.	Age & Sex (Years)	Associated Conditions	Diagnostic Basis	Boxes
II. Dextroversion					
With Congenital Cardiopathy	17	29 M	? TF or CT. Cyanotic. Bacterial meningitis. Hb. 22gms. Chest wall deformity.	Clin. X-ray. ECG	
	18	5 M	Transposition of Great Vessels (d, d-loop). High VSD. PS. Cyanotic. Hypoplastic LV. RVH. SBE. R. cavopulmonary shunt. Massive pulmonary thrombosis. Right diaphragm higher than left.	" Autopsy	
	19	1 mo. M	Tricuspid atresia without transposition. VSD. Cyanotic. Cavopulmonary shunt.	" Cath. Angios	
III. Mixed Dextrocardias					
With Congenital Cardiopathy. with Atrial Inversion	20	31 F	Corrected transposition (d, d-loop). VSD. Mild PS. Acyanotic. Regurgitation of left-sided AV valve (bicuspid). Bronchopneumonia. Systolic murmur. Mesoversion.	" Cath. Angios	
	21	14 F	Corrected transposition. VSD. PA banding in 1962. Systolic murmur. CVH. L to R shunt. Bronchopneumonia. Kyphoscoliosis.	" Cath (inc) Angios	
	22	24 F	Corrected transposition. VSD. PS. Cyanotic. RVH. Mesoversion. No menses.	" Cath (inc) Angios	
With Ventricular Inversion	23	30 F	VSD with L to R shunt. PS. Systolic murmur. RVH. ARF. Acyanotic. Ventricular trigeminy. Uterine prolapse. Cystourethrocoele; rectocele, etc.	" Cath. Angios	
	24	44 F	Polysplenia. Symmetrical liver. Complex heart anomalies. Bilateral left-sidedness. L to R shunt. PH. Inversely-related great arteries. Right diaphragm lower. Lung and liver anomalies.	" Autopsy	
IV. Indeterminate					
V. "Technical Dextrocardia" - (Levocardia)					
	25	85 F	ASHD. CHF. Af. Cardiac arrest.	Clin. ECG	
VI. Levoversion					
	26	27 F	PDA. PS. ? DORV. RVH. Cyanotic. Left diaphragm lower. Pregnant. Probably transposition of great vessels (d, d-loop) with ventricular inversion - corrected.	Clin. X-ray Cath (inc) Angios	

Af-atrial fibrillation; angios- angiocardigrams; Ao-aorta; ARF-acute rheumatic fever; ASD-atrial septal defect; ASHD-atherosclerotic heart disease; AV-atrioventricular; card-cardiomegaly; cath-catheterization; CHF-congestive heart failure; Clin-clinical; CT-corrected transposition; CVA-cerebrovascular accident; CVH-combined ventricular hypertrophy; DORV-Double Outlet Right Ventricle; ECG-electrocardiogram; F- female; FH- family history; gms-grams; Gr.-grade; H.-history; Hb-hemoglobin; HCV-hypertensive cardiovascular disease; inc-incomplete; L-liver, LA-left atrium; L to R- left to right; LV-left ventricle; LVH-left ventricular hypertrophy; M-male; MI- myocardial infarction; mo.-month; PA-pulmonary artery; PDA- patent ductus arteriosus; PH-pulmonary hypertension; PS-pulmonary stenosis; R-right; RA-right atrium; RBC's-red blood cells; R-H- right-handed; R to L- right to left; RV-right ventricle; RVH- right ventricular hypertrophy; SBE-subacute bacterial endocarditis; St- stomach; TF- Tetralogy of Fallot; VC- venae cavae; VSD- ventricular septal defect; VT- ventricular tachycardia.

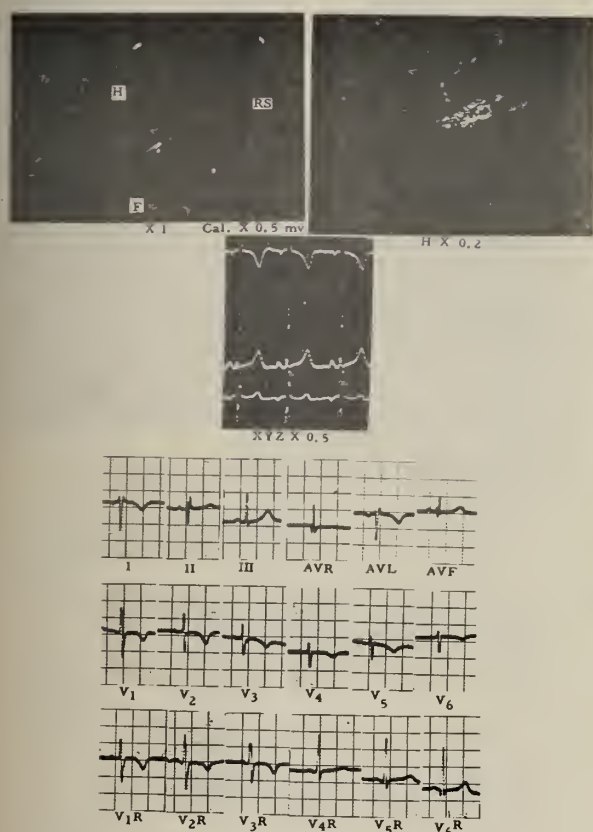


Fig. 2: Case 1. Mirrow-Image Dextrocardia, without Cardiopathy.

had a typical ECG except for (Figure 4): a deep S wave in leads I, AVL, V_{2-3} , a tall R wave in AVR, $V_{4-6}R$, a prominent S wave in LII and V_6 , prominent T wave inversions in leads II, III, AVF, V_{1-6} and diphasic T waves in the right precordial leads. A typical LVH pattern was present when the right and left arm leads were reversed. The VCG showed large H and F plane loops oriented to the right with mainly clockwise rotation in the H plane. With reversal of leads, the QRS loop was located posteriorly and to the left with figure of eight appearance in the H plane.

C. With Congenital Cardiopathy.

One patient in this group, a 60-year old male (Case 13), suffered various arrhythmias, finally requiring a temporary endocardial pacemaker. A large atrial septal defect (ASD) was confirmed by clinical and catheterization data. Autopsy showed a secundum ASD, total situs inversus, cardiomegaly with combined ventricular hypertrophy, fibrinous pericarditis and congestive heart failure. The left ventricle (LV) was described as "lying in the anterior portion and the

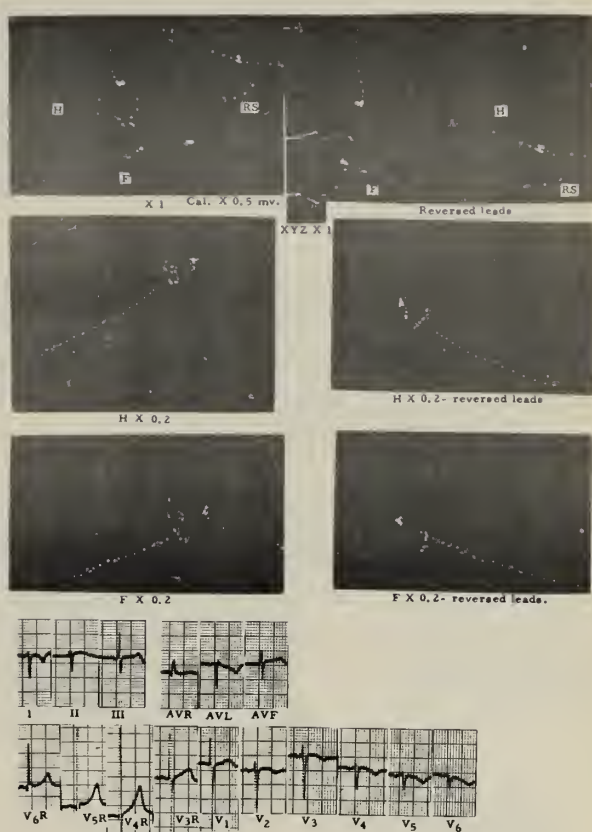


Fig. 3: Case 4. Mirrow-image Dextrocardia, without Cardiopathy.

right ventricle (RV) flat in the posterior aspect of the mediastinum" and the "semilunar valves at the same level". The ECG (Figure 5) showed atrial fibrillation and right bundle branch block (RBBB). The VCG showed the QRS loop to be located to the right, with terminal slowing to the left, anteriorly and superiorly. Very little initial anterior, leftward forces were present.

Case 14 was markedly cyanotic and was considered to have tetralogy of Fallot or Double Outlet Right Ventricle. His ECG's varied (Figure 6), with upright and inverted P waves in lead I, and right ventricular hypertrophy (RVH). The vectorcardiographic loops were located mainly to the left and anteriorly, with the initial forces oriented slightly to the left, with afferent slowing.

The catheterization study in Case 15 was consistent with tetralogy of Fallot, and a left-sided aorta; he had undergone a Brock pulmonary valvotomy. His ECG (Figure 7) showed a markedly left, superior QRS axis and suggested a large left-sided LV and a right-sided RV. The P waves changed from inverted to upright

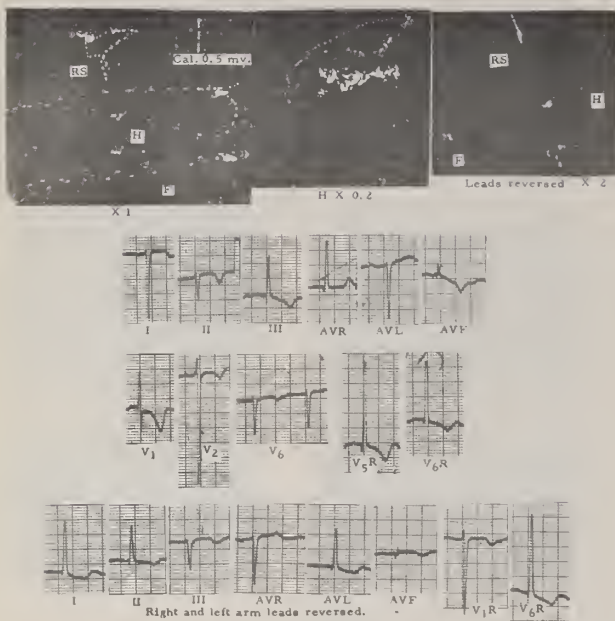


Fig. 4: Case 11. Mirrow-Image Dextrocardia, with Acquired Cardiopathy-LVH.

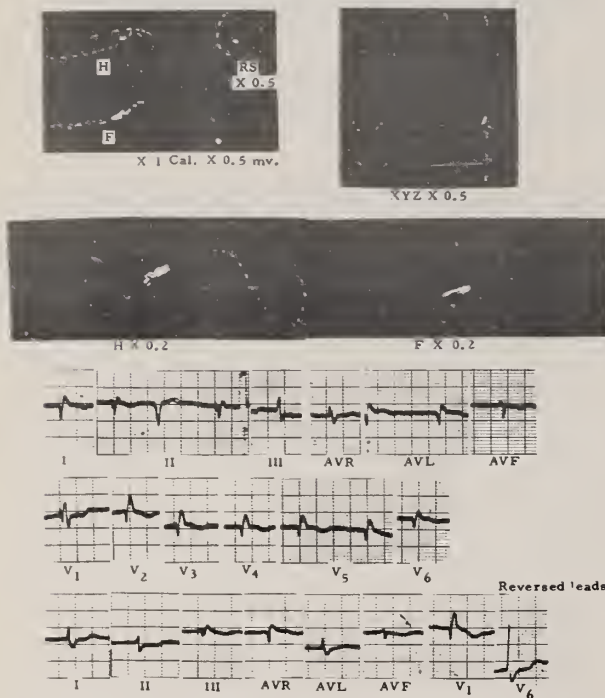


Fig. 5: Case 13. Mirrow-Image Dextrocardia, with Congenital Cardiopathy. Atrial septal defect. Atrial fibrillation. RBBB.

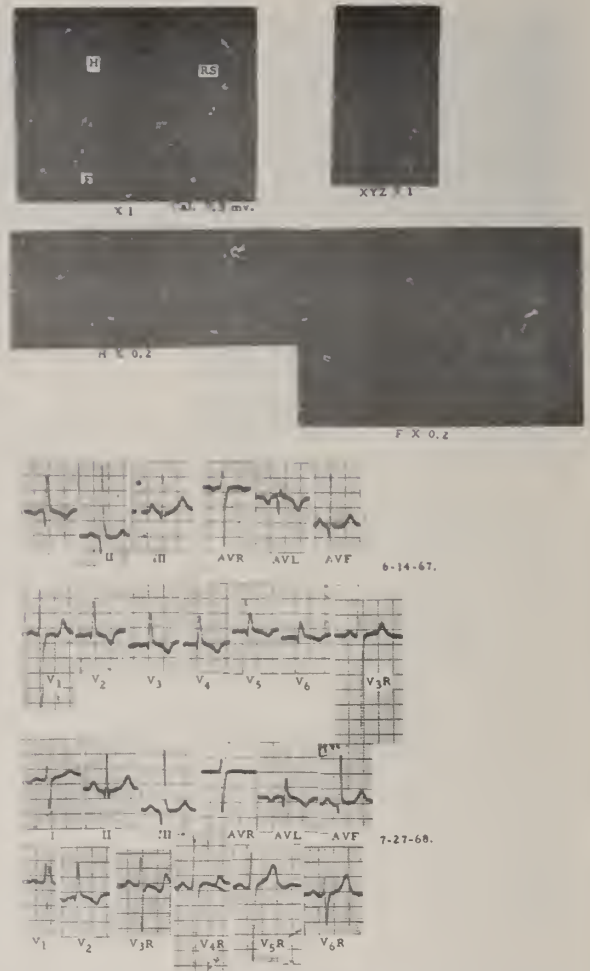


Fig. 6: Case 14. Mirrow-Image Dextrocardia, with Congenital Cardiopathy. Tetralogy of Fallot or Double Outlet Right Ventricle.

in the same lead I strip. The VCG showed a counter-clockwise QRS loop located to the left and superiorly. The P waves were inverted in leads I, AVL, and up-right in AVF, in 1959 (some 9 years previously). Likewise, the ECG's suggested the LV to be located leftward and the RV to be located rightward in Cases 14 and 16.

Case 16 was one of tetralogy of Fallot or Taussig-Bing anomaly. However, his ECG (Figure 8A) showed a qR in the left precordial leads and a qrs in V₇R and an r/s complex in V₆R. Arrhythmias and P wave changes were noteworthy (Figure 8B). The QRS loops were small, located both to the right and left.

Mirrow-image dextrocardia consists of classical mirrow-image dextrocardia with inversely related great arteries (Cases 1-10), mirrow-image dextrocardia with

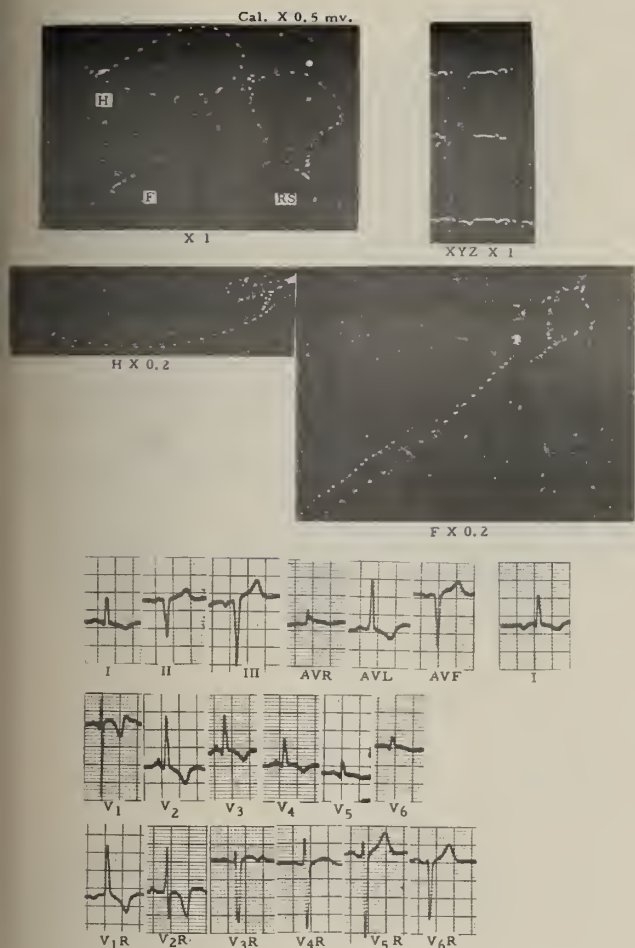


Fig. 7: Case 15. Mirrow-Image Dextrocardia, with Congenital Cardiopathy. Tetralogy of Fallot.

complete transposition of the great arteries (1-transposition), and mirrow-image dextrocardia with corrected transposition (1-transposition) (Cases 20-22)(1).

II. Dextroversion. With Congenital Cardiopathy.

Case 17 was suspected of having a ventricular septal defect (VSD) and pulmonary stenosis (PS). The QRS axis (Figure 9) was superiorly directed. The QRS loops were located posteriorly, superiorly and to the right; afferent slowing was present. The initial vector went directly to the right.

Only ECG's were available for study in Case 18. This boy had associated lesions of transposition of the great arteries, a large VSD, ASD, PS and had undergone a cavopulmonary anastomosis. The QRS axis (Figure 10) was markedly superior, to the right and posteriorly.

The QRS axis was also located markedly superior, to the right and posterior in Case 19 (Figure 11). A cavo-

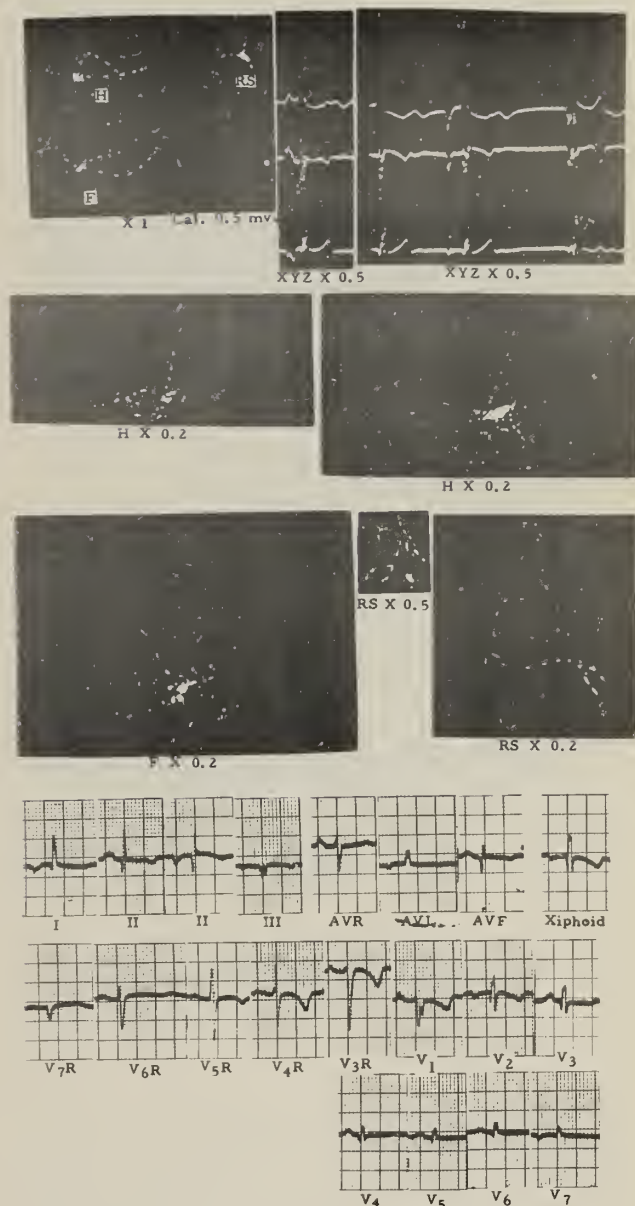


Fig. 8A. Case 16. Mirrow-Image Dextrocardia, with Congenital Cardiopathy. Tetralogy of Fallot or Taussig-Bing Anomaly.

pulmonary shunt had been done for Tricuspid Atresia, and a VSD.

Deep Q waves were present in leads I, II and III in 2 cases, (the other case having only tiny r's in II, III), and in AVL in one case; this has been emphasized before in dextroversion. A clockwise frontal, superior QRS loop may suggest an Atrioventricular canal defect.

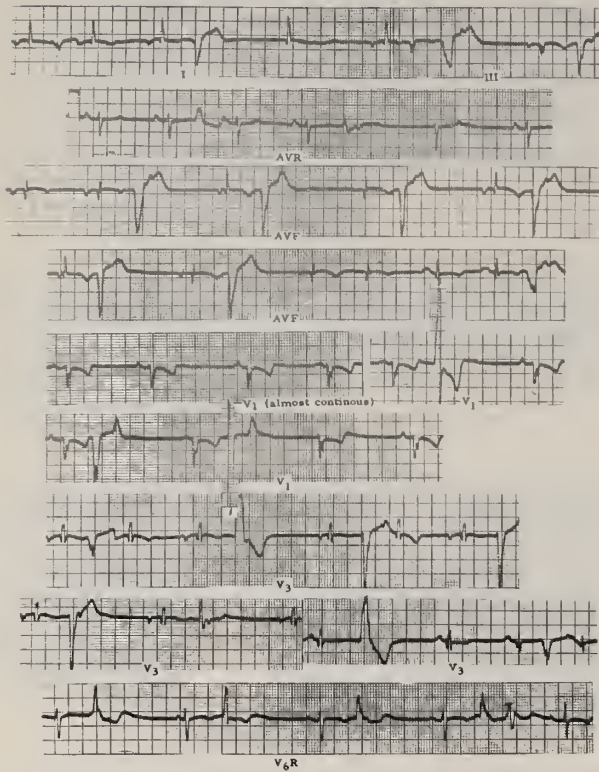


Fig. 8B: Case 16. Electrocardiographic strips showing arrhythmias and P wave changes.

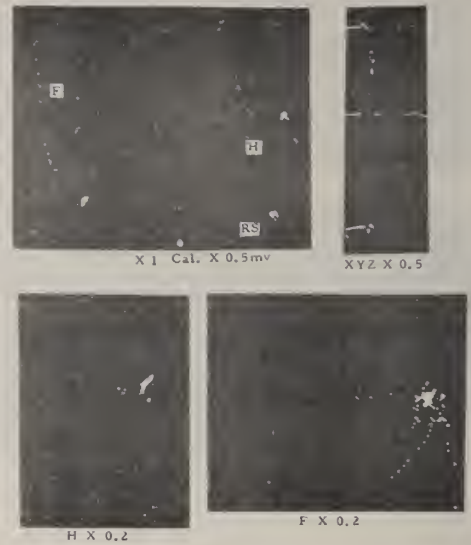


Fig. 9: Case 17. Dextroversion ?? with Congenital Cardiology. PS. VSD.

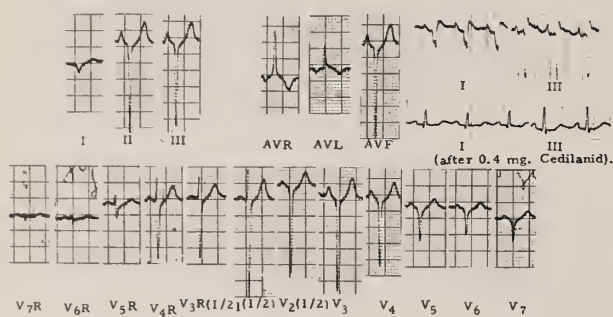


Fig. 10: Case 18. Dextroversion, with Congenital Cardiology. Transposition of Great Vessels, PS. VSD.

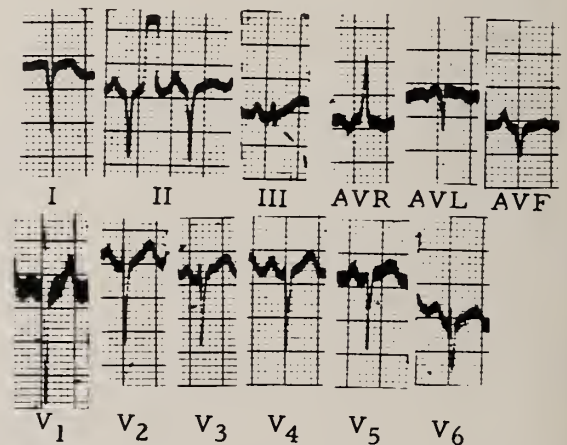


Fig. 11: Case 19. Dextroversion, with Congenital Cardiology. Tricuspid Atresia. VSD. Cavopulmonary Shunt.

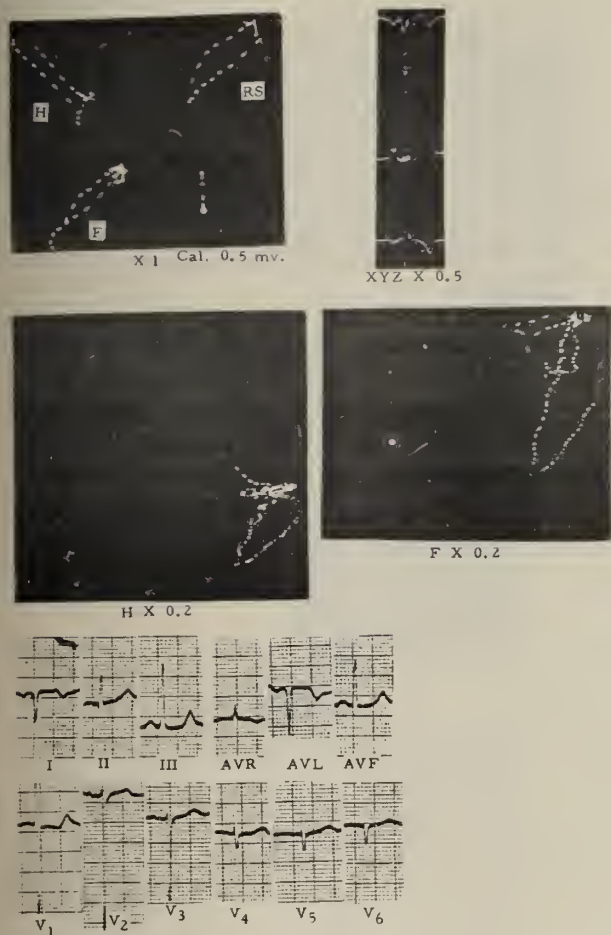


Fig. 12: Case 20. Mixed Dextrocardia, with Atrial Inversion. (Corrected transposition.-d; D-loop). VSD.

Dextroversion was present in 47 percent of Van Praagh's cases of dextrocardia and was the commonest type of dextrocardia (1). Normally related great vessels were found in 18 percent and corrected transposition (1-transposition) in 29 percent of the cases. The latter has been called dextrocardia with inverted transposition by Spitzer and mixed dextrocardia with ventricular inversion by Lev.

III. Mixed Dextrocardias. A. With Atrial Inversion.

These three cases all had corrected transposition (d-transposition, d-loop). Ventricular septal defects were present in all, and PS in two. Mesoverision was present in Cases 20 and 22. Situs inversus existed. Catheterization revealed regurgitation of the left-sided AV valve (bicuspid) in Case 20.

The ECG (Figure 12) of Case 20 was similar to that of a mirror-image dextrocardia, but a deep S wave was

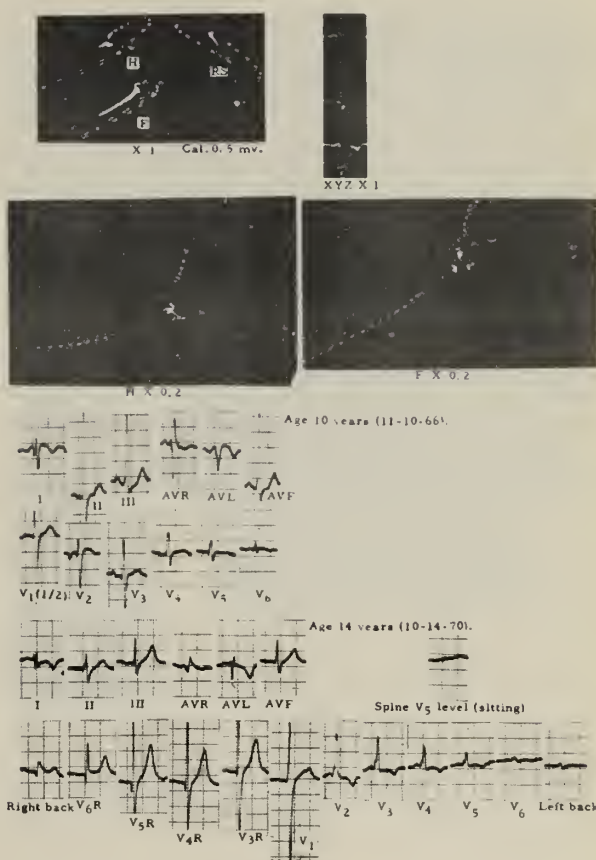


Fig. 13: Case 21. Mixed Dextrocardia, with Atrial Inversion. VSD.

present in V_{1-2} , and there was, in general, a QS complex in V_6 . The QRS loops were oriented mainly to the right, posteriorly and inferiorly, with predominantly clockwise rotation. The initial vector was to the right and anteriorly.

In Case 21, the P waves and QRS complexes (Figure 13) were different on two tracings taken 4 years apart. The vector loops occupied all spatial directions. The initial vector was oriented to the left. There was late slowing, posteriorly, leftward and superiorly.

Case 22 was cyanotic. The great vessel and ventricular anatomy was difficult to identify with catheterization and angiography. Complexes of r/s type were seen in V_6R , and qR type in V_6 (Figure 14). The QRS loops were mainly located posteriorly and to the left, associated with afferent slowing. There was clockwise rotation in the H and RS planes and counterclockwise rotation in the F plane.

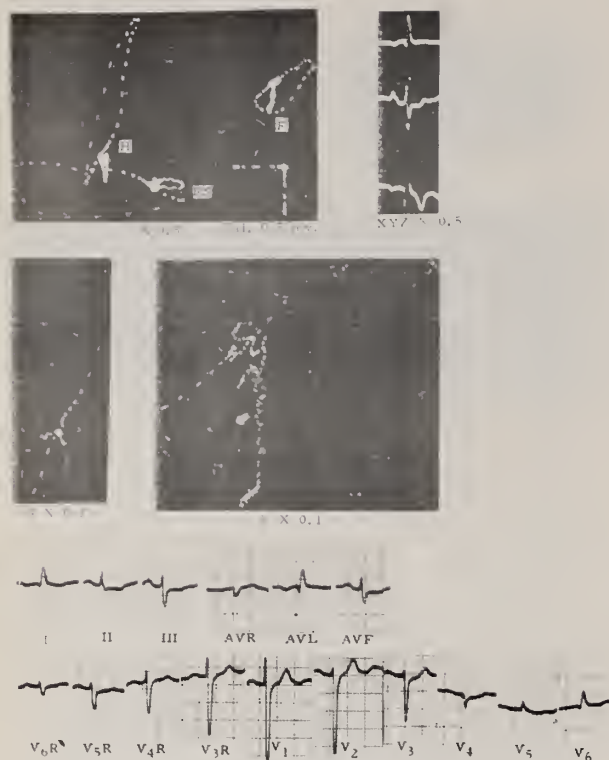


Fig. 14: Case 22. *Mixed Dextrocardia, with Atrial Inversion. PS. VSD.*

The maximal QRS vectors in the H. and F. planes in the above 3 cases were: $+225^{\circ}$, $+142^{\circ}$, -75° and $+131^{\circ}$, $+145^{\circ}$, -22° , respectively.

B. With Ventricular Inversion.

Case 23 was classified in this category (corrected transposition-1-transposition, 1-loop). This might be called also dextroversion with corrected transposition. A VSD and PS were present, as has been noted by others before. The QRS axis (Figure 15) was superior; the ECG, however, suggested the RV to be on the left, and the LV on the right. The vectorcardiographic QRS loops were left and superior, including the initial vector. Early and afferent slowing was present. Situs solitus was present.

The difficulty of differentiating dextroversion from mixed dextrocardia with ventricular inversion, short of an autopsy examination, has been noted (7). In the former the aorta originates from a left-sided LV and makes a wide aortic loop convex to the right; while in the latter the aorta originates from a left-sided RV, is situated anteriorly and makes a narrow aortic loop convex to the left.

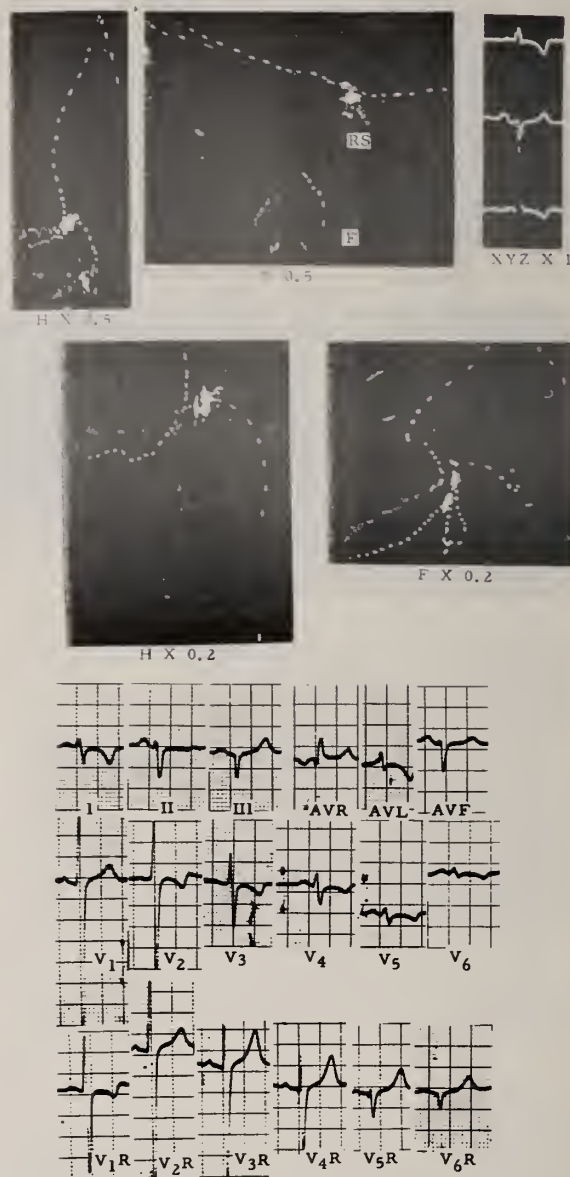


Fig. 15: Case 23. *Mixed Dextrocardia, with Ventricular inversion.*

IV. Indeterminate Situs.

A 44-year old female, Case 24, demonstrated the interesting syndrome of Polysplenia, a midline liver, atrial isomerism, pulmonary and systemic venous anomalies, and anomalies of the lung (bilateral left-sidedness). Her case (autopsied) is the subject of a separate report.

The ECG (Figure 16) revealed varied complex arrhythmias. A QR complex was present in lead I and AVL, and R/S in V_6R and an $rsR's'$ in V_6 .

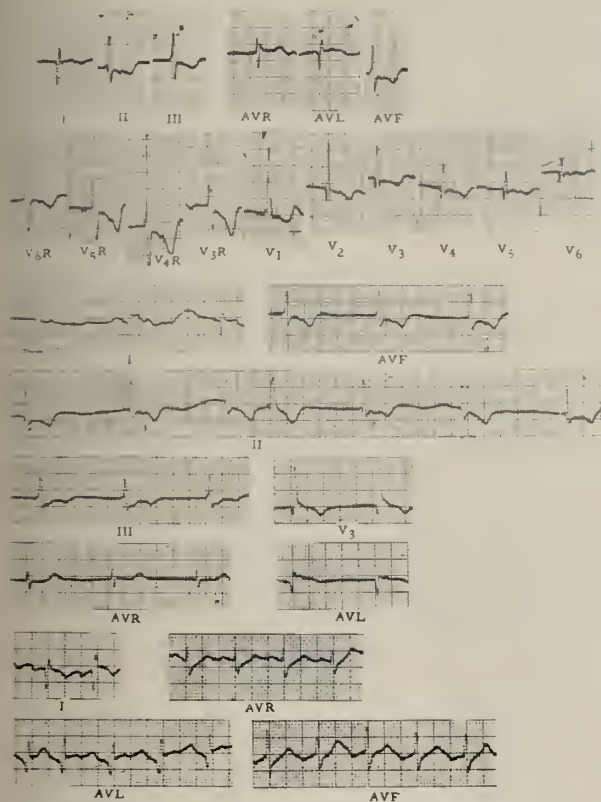


Fig. 16: Case 24. Indeterminate Situs. Polysplenia. Atrial Isomerism. 16 leads plus ECG rhythm strips.

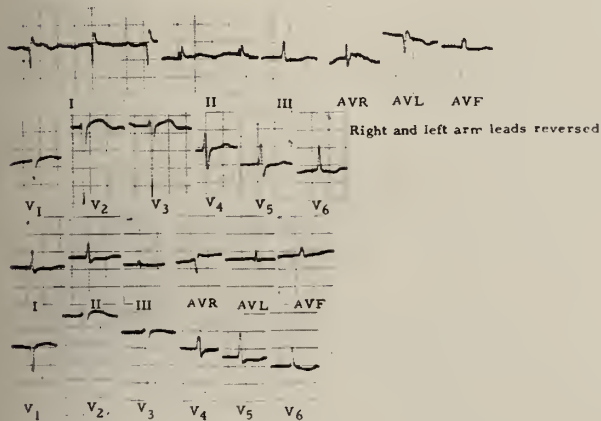


Fig. 17: Case 25. "Technical Dextrocardia" - levocardia. Atherosclerotic heart disease. Atrial fibrillation. Congestive heart failure.

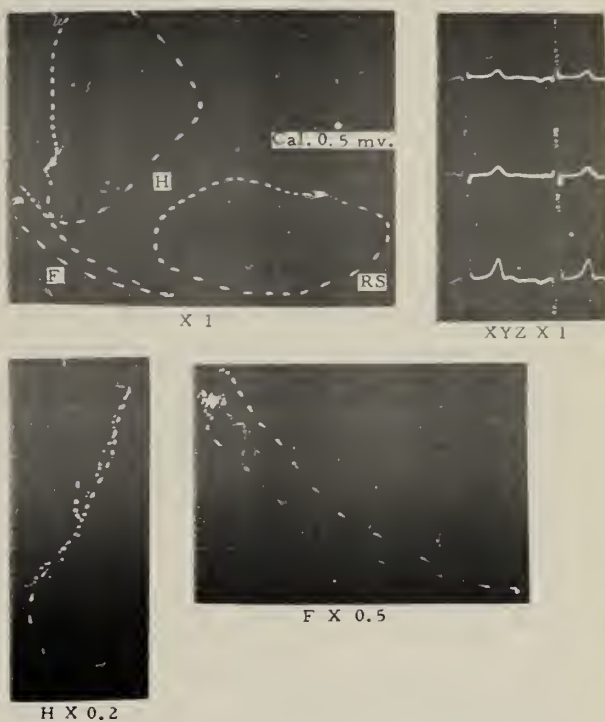


Fig. 18: Case 26. Levoersion, with Congenital Cardiology. Probably Corrected Transposition (d-transposition, d-loop). PDA. PS. Possible Double Outlet Right Ventricle.

V. "Technical Dextrocardia".

This patient, Case 25, had an unusual initial tracing (Figure 17) due to reversal of the right arm and left arm electrode wires. This was readily evident by the normal precordial lead pattern and repetition of the tracing. A slight terminal conduction defect was seen. Atrial fibrillation was present, thus the value of P wave polarity was not available. Technical dextrocardia has a QRS transition in the precordial leads, and the P waves are not inverted in leads V₂₋₆.

VI. Levoersion.

This rare malposition was uncovered in a 27-year old cyanotic female (Case 26) who was pregnant. Transposition of the great arteries (d) and probably ventricular inversion were present. Patent ductus arteriosus, PS and possible Double Outlet RV were associated lesions.

The VCG QRS loops (Figure 18) were located mainly to the left, inferiorly and posteriorly, with a small initial rightward vector. The H and F plane loops rotated counterclockwise and the RS plane loop clockwise.

No cases of dextrocardia were included in this series.
(To be continued)

MULTIPLE SCLEROSIS IN PUERTO RICO (EXPERIENCE AT THE UNIVERSITY HOSPITAL. I. *Review of a Series of Cases.*

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Miguel Fiol, MS IV
Pedro Cedó, MS IV

Multiple sclerosis is one of the primary demyelinating diseases poorly understood and characterized by patchy but multiple areas of demyelination of the central white matter. It is a chronic progressive degenerative process with a variable clinical course and a variety of neurological signs and symptoms with a tendency to remission and exacerbation.

This condition was first described by Cruveilhier (1) in 1835 and later on by Charcot (2) to whom we owe the best early description of this illness. He spoke of the triad of intention tremor, nystagnus and scanning speech often referred to as the Charcot triad in memory of this famous French neurologist.

It is a fairly common neurological disease in cold climates, with a lower incidence in the tropics (3).

This project was undertaken with the purpose of determining the frequency, clinical manifestations; age, race and sex distribution and other interesting aspects of multiple sclerosis in Puerto Rico.

Method and Procedure

All patients being followed at the Neurology Clinic of the University District Hospital with a diagnosis of multiple sclerosis were given a new appointment and a thorough neurological and physical examination was conducted in 7 cases of a total of 20. The other 13 did not attend the interview because of diverse reasons. The records of these 13 were reviewed and 9 cases were selected. Cases selected were those which had been completely worked up and had been followed for a minimum of 2 years. A total of 16 cases were utilized in this investigation.

The diagnostic criteria utilized in the cases reviewed is that of Mackay (4) (1950) which includes the following:

1. onset of symptoms between 15-30 years.
2. dissemination of the lesion in space.
3. dissemination of the lesion in time (remission and exacerbation).
4. generally increasing disability.
5. absence of clinical and serological evidence of lues.

Results

The data obtained after analyzing the above mentioned 16 cases of proven multiple sclerosis are con-

tained in the following tables:

TABLE I: AGE DISTRIBUTION

Age Group	Number
Group I - 1-12	0
Group II - 13-21	2
Group III - 22-35	6
Group IV - 36-48	7
Group V - 49-61	1
Total No. Cases	16

TABLE II: AGE OF ONSET AND SEX DISTRIBUTION

Age in Years	Males	Females	Total
Below 12	0	0	0
12-22	0	3	3
23-30	4	3	7
Over 31	2	4	6
Total No. Cases	6	10	16

TABLE III: RACE DISTRIBUTION

Race	Number
White	13
Colored	2
Unknown	1

TABLE IV: FREQUENCY OF OCCURRENCE OF VARIOUS SYMPTOMS AT ONSET OF MULTIPLE SCLEROSIS

Symptom	Percentage
Paresthesias and numbness	69 percent
Diplopia	44
Weakness of extremities	37
Impaired visual acuity or loss of vision	25
Ataxia	18
Dizziness or vertigo	18
Pain in eye	13
Headache	13
Sphincteric impairment	13
Hyperesthesia	6.3
Scanning of speech	6.3
Seizures	0

TABLE V: FREQUENCY OF OCCURRENCE OF VARIOUS NEUROLOGICAL SIGNS IN MULTIPLE SCLEROSIS

Symptom	Percentage
Weakness of lower limbs	94 percent
Ataxia	88
Nystagmus	81
Sphincteric impairment	63
Loss of visual acuity	56
Positive Romberg Test	56
Extensor Plantar Response	56
Intention tremors	50
Absence of abdominal superficial reflexes	50
Optic atrophy or pallor of disk	37
Scanning of speech	37
Diplopia	31
Strabismus	18
Central Scotomata	18
Internal ophthalmoplegia	13
Memory loss	6.3

TABLE VI: DISTRIBUTION OF PROTEIN VALUES IN CEREBRO-SPINAL FLUID

M. per 100 ml.	Number
20-30 mg percent	1
31-40 mg percent	4
41-50 mg percent	2
51-60 mg percent	4
greater than 60 mg percent	3
Total	14

TABLE VII: RELATIONSHIP OF ONSET M. S. WITH VISIT TO USA

Never visited prior to onset	1 case
Living at U. S. A. at time of onset	7 cases
Just returned from U. S. A.	2 cases
Total -	10 cases

Discussion

If we compared the clinical picture of patients with multiple sclerosis in Puerto Rico, with a group of cases in Continental U. S. A., there is no significant difference between them.

Kurland (5, 6) estimates a prevalence rate in the United States of 10 per 100,000 in the Southern part to about 50 to 75 per 100,000 in Northern areas.

The incidence rate has been reported equal in colored and white races, yet it is rare in Africa and in our series the majority are white.

In our series there are 6 males and 10 females. Mc-Alpine, Compston and Lumsden (7) demonstrate a slightly more common incidence in females.

In the series of Carter, Sciarra and Merritt (8) the majority of cases fall in the age group from 21 to 40. In our series the majority of cases occurred between 22-48.

The four most common signs and symptoms in our cases are compared to that of Carter, Sciarra and Merritt as shown in the following tables:

TABLE VIII

Symptoms:		
<i>Carter et al</i>		<i>Our Series</i>
1. Weakness	54 percent	37 percent
2. Paresthesias	32	68
3. Diplopia and Impaired visual acuity	21	43
4. Tremor and Ataxia	19	18

TABLE IX

Signs:		
<i>Carter et al</i>		<i>Our Series</i>
1. Extensor plantar response	89 percent	74 percent
2. Absent abdominal reflexes	70	87
3. Weakness	69	93
4. Nystagmus	68	81

The difference between the two series is most likely due to the marked difference in the number of cases, ours is a very small series compared to the large series of Carter et al, which consists of over 500 cases.

A very significant finding is the fact that 9 out of 10 of our cases had the onset while living or recently returning from the colder climate of U. S. A.

In a recent research investigation, Leibowitz and Alter (9) found a similar finding of higher incidence among European emigrants to Israel than among local resident group.

In our small series of cases the use of ACTH, systemic steroids and intrathecal steroids, apparently failed to alter the natural course of the illness. During acute exacerbations some cases showed improvement with the use of the above medications. However the evolution of signs and symptoms following the treatment is not apparently different to non treated cases.

Summary

The experience at the University Hospital in a series of 16 selected cases of multiple sclerosis is reported. The case histories and the clinical findings are carefully studied with an analysis of the following: age distribution, age of onset, sex and race distribution, frequency of occurrence of neurologic signs and symptoms, protein values in CSF and relationship of onset to visit to U. S. A.

Our clinical series is compared with the observations of McAlpine et al and Carter et al, demonstrating the

similarity of multiple sclerosis cases in Puerto Rico with the other series.

A significant finding is the observation that 9 out of 10 of our cases had the onset while living in the U. S. A. or after recently returning to Puerto Rico.

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THE MANAGEMENT OF ACUTE SCROTAL SWELLING IN CHILDREN AND YOUNG ADULTS

Roberto F. Fortuño, MD

For many years, the general understanding among local physicians was that acute torsion of the testis occurred rarely in Puerto Rico. This diagnosis was recorded only three times in the operating room files of the San Juan City Hospital from July 1, 1957 to June 30, 1961 (1).

Many children were seen in our Emergency Room with acute swelling of the scrotum accompanied sometimes by fever, pain and local erythema. In most of these cases the diagnosis of acute epididymitis was reached and the child treated accordingly. Because of our large patient load and limited facilities, their final outcome was never known as most of these children were lost to follow up.

Early in 1968 we were impressed by discovering two boys with advanced bilateral testicular atrophy, resulting from consecutive episodes of torsion of their spermatic cords. In both cases, well trained physicians had misdiagnosed their first attack. We reacted by establishing a strict, new rule: All acute scrotal swelling in children were to be explored as an emergency. The diagnosis of acute epididymitis was to be made in the operating room.

Our findings were striking. The first six patients explored with this syndrome proved to have acute torsion of either the testicle or one of its appendages. We began to doubt if epididymitis existed in children at all. This condition was finally found in our seventh and eighth cases.

After three years of exploring all the patients with acute scrotal swelling in our service, we thought it would be wise to review the cases, analyse our findings and present them in this short article.

Clinical Material

We have reviewed the clinical record of all the patients

that were subjected to scrotal exploration in the urological service of the Puerto Rico Medical Center and a local private hospital from July 1968 to October 1971.

The operations were performed by various physicians in thirty different individuals. Six of them were private cases.

Table 1 illustrates the operative findings. Our series includes 12 cases with testicular torsion, seven patients with torsion of an appendix, eight epididymitis and three miscellaneous conditions.

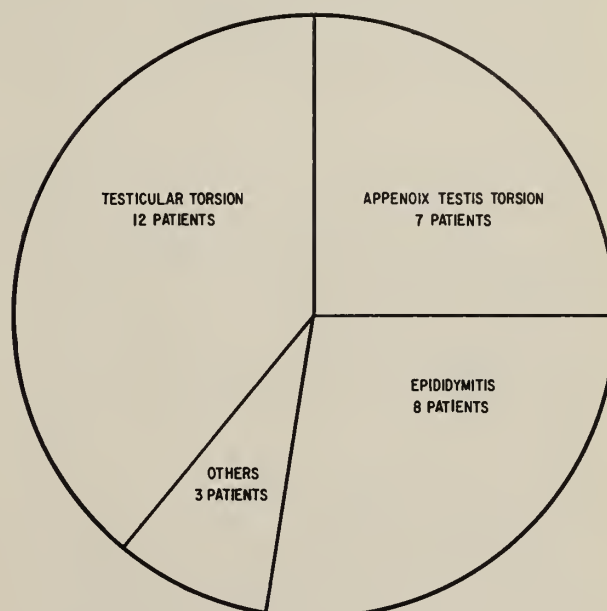
The age distribution is shown in Table 2.

All of our patients presented very similar clinical pictures (Table 3). Pain, edema and erythema of the involved scrotum was present in all of them. We could find no specific sign or laboratory finding to distinguish between the different clinical entities.

Table 4 presents the location of the scrotal pathology. Testicular torsion appeared more often on the left while the appendix testis was affected only on the right. No significance is given to these findings.

The accuracy of the preoperative diagnosis is illustrated in Table 5. We were able to make an accurate clinical diagnosis in only 26 percent of the cases. In a large percentage

TABLE 1: OPERATIVE FINDINGS



From the Department of Urology, San Juan Municipal Hospital, San Juan, Puerto Rico.

TABLE II: AGE DISTRIBUTION

	Youngest	Oldest	Average Age	Total
Testicular Torsion	1 yr.	22 yrs.	11.5 yrs.	12
Appendix Testis Torsion	2 mos.	13 yrs.	9.0 yrs.	7
Epididymitis	1 mo.	19 yrs.	8.8 yrs.	8
Other	2 yrs.	15 yrs.		3

TABLE III: PRESENTING SIGNS AND SYMPTOMS

	Testicular Torsion	Appendix Testis Torsion	Epididymitis	Others
Presenting Signs and Symptoms	Swelling Redness Pain scrotum	Swelling Redness Pain Scrotum Black dot sign in 1 case	Swelling Redness Pain Scrotum	Swelling Redness Pain Scrotum Black dot sign in one case
Urinalysis	Infection in 1 case	Negative in all	Infection in 1 case	Infection in 1 case
WBC	7,200-16,523	5,200-12,370	9,001-12,400	10,400-12,340
Hgb	10.8-15.3 gms	10.2-13.5 gms	10.2-12.4 gms	8.7-12.5 gms
Fever	1 case	None	None	None
Average duration of symptoms	5.63 days	5.95 days	4.1 days	5.6 days
Average hospitalization	3.66 days	3.48 days	3.12 days	4.66 days
Post Op. Complications	None	None	None	None

TABLE IV

	Right	Left	Bilateral	Total
Testicular Torsion	2	9	1	12
Appendix Testis Torsion	7	-	-	7
Epididymitis	3	5	-	8
Para Testicular Tumor	-	1	-	1
Cellulitis of the Scrotum	-	1	-	1
Incarcerated Inguinal Hernia	1	-	-	1
Total -	13	16	1	30

TABLE V

Preoperative Diagnosis		Postoperative Diagnosis		Percent Correct
Testicular Torsion	16	Testicular Torsion	7	43 Percent
Epididymitis	1	Appendix T. Torsion	1	0 Percent
Appendix Testis Torsion	2	Appendix Testis Torsion	1	50 Percent
		Scrotal Cellulitis	1	
Undetermined	10	Testicular Torsion	5	0 Percent
		App. Test Torsion	2	
		Epididymitis	3	
Total Operated	30	Correct Diagnosis	8	26.6 Percent

of our patients the surgeon had no definite preoperative diagnosis. This confirms the similarity in the clinical picture of the different clinical entities.

Of the patients with testicular torsion six were explored within the 24 hours of their disease and all six were found to have viable testis and orchidopexy could be performed. In the other six patients explored after the first 24 hours the infarcted testis had to be removed.

Discussion

Most text books describe torsion of the testis as a condition which starts with a sudden sharp bout of pain in contrast with the less acute onset of epididymitis (2, 3). Supposedly the pain in the twisted cord is increased by elevation of the testis, while some alleviation is achieved in a boy with acute epididymitis by the same maneuver. (Prehn sign). It is said that in the twisted cord the epididymitis lies anterior to the testis while in epididymitis it is palpated in its normal posterior position. We are told that in torsion the testis lies in a more horizontal position while the infected organ is more freely movable in the scrotal cavity. None of these signs were of diagnostic aid in our patients. Palpation of an acute swollen scrotum is not easy and we have yet to find a method of determining variation in the intensity of pain in a screaming child.

We were very impressed by the similarity of the clinical findings in all cases regardless of the diagnosis. The degree of scrotal edema, the intensity of the erythema, the pain distribution varied from case to case, but was not related to the underlying cause.

To our surprise none of the eight cases with epididymitis presented evidence of other active genitourinary infection and in only one the temperature was elevated. They had no complications from the surgical

exploration and we were able to discharge them in less than three days. The epididymitis was not aggravated by the surgical exploration.

Torsion of the appendix testis was encountered in seven children. In these cases the inflammation tended to be more localized but on several occasions this finding completely misled the examining physician in determining the initial diagnosis.

The importance of early operation in children with a twisted cord is dramatically illustrated in our series. We were able to spare the testis in all our patients with twisted cords explored within the first 24 hours. This is a well known fact previously established by many authors (4, 5, 6). In order to preserve testicular function one must operate early.

Conclusions

1. Until better diagnostic methods are developed, all children with acute scrotal swelling should be suspected of having an infarcted testis.
2. The differentiation between acute epididymitis and torsion of the spermatic cord by clinical means is most difficult.
3. We strongly believe in early exploration of all acute scrotal swelling presenting in children and young adults.

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LEY QUE REGULA LA PRACTICA DE LA
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Ley Núm. 22

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(Según quedó enmendada por la Ley Núm. 61 de 22 de abril de 1958, Núm. 97 de 21 de junio de 1961; Núm. 17 de 11 de junio de 1965; Núm. 127 y 135 de 28 de junio de 1969; Núm. 147 de 30 de junio de 1969; Núm. 75 de 30 de mayo de 1970 y Núm. 18 de 24 de abril de 1972).

Para regular el ejercicio de la profesión médica en Puerto Rico; para establecer un Tribunal Examinador de Médicos; para derogar la "Ley estableciendo un Tribunal Examinador de Médicos, regulando el ejercicio de la profesión médica, y para otros fines". Aprobada el día 30 de julio de 1923; para derogar la "Ley para enmendar la Ley titulada "Ley estableciendo un Tribunal Examinador de Médicos, regulando el ejercicio de la profesión médica y para otros fines, aprobada en 30 de julio de 1923; y para otros fines", aprobada el día 1ro. de julio de 1924, y para otros fines.

Decrétase por la Asamblea Legislativa de Puerto Rico:

"Artículo 1. Al empezar a regir esta ley, el Gobernador de Puerto Rico, por y con el consejo y consentimiento del Senado de Puerto Rico, a propuesta de las sociedades o asociaciones médicas, debidamente inscritas en el Departamento de Estado de Puerto Rico, como sociedades o asociaciones para fines no pecuniarios, nombrará por un término de cuatro años, un Tribunal Examinador de Médicos, compuesto de siete médicos, con no menos de cinco años de ejercicio de la profesión en el Estado Libre Asociado cada uno, y de acuerdo con las siguientes disposiciones: Disponiéndose, que no más de tres de estos médicos serán residentes de la ciudad de San Juan, y disponiéndose, además, que para los exámenes de podiatría se añadirá al Tribunal un podiatra nombrado por el Gobernador con el consejo y consentimiento del Senado de Puerto Rico, a propuesta de la sociedad o asociación de Podiatras de Puerto

Rico, debidamente inscrita en el Departamento de Estado del Estado Libre Asociado como sociedad o asociación de fines no pecuniarios".

"Artículo 2. Dicho tribunal se proveerá de un sello oficial y elegirá de su seno, en la primera sesión y cuando hubiese una vacante, un Presidente y 6 vocales. Cuatro miembros del Tribunal constituirán quorum y las decisiones se tomarán por mayoría".

"Artículo 3. El Presidente y el Secretario de Estado firmarán todo documento oficial emanado del Tribunal Examinador de Médicos".

"Artículo 4. El Tribunal tendrá a su cargo la autorización, en el Estado Libre Asociado de Puerto Rico, de acuerdo con las disposiciones de esta ley, del ejercicio de la profesión de médico-cirujano, podiatra, osteópata y de las profesiones auxiliares, quedando por la presente autorizado para expedir licencias para las profesiones siguientes: de médico-cirujano, de osteópata, de podiatra, de practicante de enfermera obstetra o comadrona. Disponiéndose, que para la autorización del ejercicio de la podiatría en Puerto Rico el Tribunal quedará compuesto por dos de los médicos y el podiatra."

"Artículo 5. El Secretario de Estado rendirá al Secretario de Hacienda una cuenta mensual de sus ingresos y gastos y certificará la asistencia por sesiones de los miembros del Tribunal; deberá llevar un libro de actas de las sesiones, las cuales firmará juntamente con el Presidente, y también tendrá a su cargo un registro de todos los solicitantes de licencias, debidamente clasificados por profesiones, con la expresión de la edad de los mismos, el tiempo invertido en sus estudios y el nombre y lugar de las instituciones que expidieron los diplomas correspondientes, o los certificados de asistencia y práctica. También se hará constar en dicho registro si ha sido rechazado el aspirante o si ha recibido alguna licencia con arreglo a esta ley. Además tendrá a su cargo y bajo su custodia y responsabilidad todos los documentos, libros de registros y archivos pertenecientes

al Tribunal.”

“Artículo 6. El Tribunal presentará al Gobernador de Puerto Rico, por conducto del Secretario de Estado, un informe anual demostrativo de sus trabajos, dando cuenta del número de solicitudes recibidas y licencias expedidas; de las cuentas de gastos e ingresos; cuentas de dietas recibidas por los miembros del Tribunal y quiénes las recibieron, y los demás datos que el Gobernador solicitare”.

“Artículo 7. El Tribunal podrá contratar los servicios de un abogado en casos en que lo estime necesario; y los honorarios serán satisfechos de los fondos del Tribunal Examinador de Médicos; y si éstos no fueren suficientes, de cualesquiera otros fondos existentes en el Tesoro Estatal, no destinados para otras atenciones; tendrá facultad para citar testigos y obligarlos a comparecer ante él, y estará asimismo facultado para tomar declaraciones y juramentos y para recibir las pruebas que le fueren sometidas en todo asunto que caiga dentro de su jurisdicción. Asimismo podrá exigir que se le envíen copias de libros, documentos o extractos de ellos, en todos los casos en que tenga derecho a examinar los originales o a exigir la presentación de los mismos. Toda citación con apercibimiento expedida por el Tribunal, deberá llevar el sello del mismo, y deberá ser suscrita por el Presidente o el Secretario de Estado, pudiendo ser notificada por cualquier adulto en cualquier parte del Estado Libre Asociado de Puerto Rico.”

“Todo testigo que fuere requerido para comparecer ante el Tribunal o ante cualquiera de sus miembros, recibirá por cada día de comparecencia la suma de cinco (5) dólares y recibirá además quince (15) centavos por cada milla recorrida por el testigo, por la ruta usual, entre su casa y el sitio de la comparecencia. Todos los desembolsos que se hicieren en el pago de dichos honorarios se pagarán en la misma forma que se dispone en el primer párrafo de este artículo.”

“Los honorarios para notificación de una citación con apercibimiento, serán iguales a los que se pagan por servicios similares en el Tribunal Superior. Los honorarios, gastos y costas en cualquier audiencia o en relación con ella serán satisfechos en la forma que el Tribunal acordare.”

“Si cualquier individuo que hubiere sido citado con apercibimiento para comparecer ante el Tribunal o ante cualquiera de sus miembros, dejare de obedecer dicha orden o citación, o si cualquier individuo que compareciere ante el Tribunal o ante cualquiera de sus miembros se negare a prestar juramento o a declarar, o a contestar cualquier pregunta pertinente,

o a presentar cualquier documento pertinente cuando así lo ordenare el Tribunal, éste podrá invocar la ayuda de cualquier Sala del Tribunal Superior de Puerto Rico, para obligar dicha comparecencia, la declaración de los testigos y la presentación de documentos; y dicha corte por causa justa demostrada, expedirá una orden a cualquier persona para que comparezca ante el Tribunal o cualquiera de sus miembros y presente los papeles y documentos requeridos, si así se le ordenare, y para que preste declaración en cuanto al asunto de que se trate; y la falta de obediencia a dicha orden de la corte, constituirá desacato y podrá ser castigada como tal”.

“El Tribunal podrá promulgar las reglas y reglamentos que estime conveniente para la buena marcha de dicho organismo, y para el mejor cumplimiento de esta Ley, siempre que aquellos no estuvieren en pugna con la misma, ni impidan el cumplimiento de los deberes específicos en ella establecidos. Tales reglas y reglamentos, una vez aprobados por el Tribunal, tendrán fuerza de ley y serán promulgados y publicados por el Secretario de Estado de Puerto Rico.”

“Artículo 8. A cada miembro del Tribunal, por la presente, se le asigna la suma de treinta y cinco (35) dólares por cada día o fracción que prestare sus servicios y, además, a los no residentes se les pagará millaje, a razón de quince (15) centavos por cada milla recorrida.”

“Artículo 9. Toda persona que fuere convicta de ejercer ilegalmente la medicina o cirugía, la osteopatía, o cualquiera de las profesiones auxiliares reguladas por esta ley, conforme a las disposiciones de esta ley, incurrirá en delito menos grave y será castigada con una multa no menor de mil (1,000) dólares o cárcel por un mes, o ambas penas a discreción del Tribunal. En caso de reincidencia el delito aparejará pena mínima de noventa días de cárcel. El Tribunal Superior tendrá jurisdicción concurrente sobre estos casos.”

“Para los efectos de esta ley, se considerará como ejerciendo ilegalmente la medicina y cirugía, la osteopatía, o cualquiera de las profesiones auxiliares reguladas por esta ley o cualquier persona que sin poseer una licencia expedida por el Tribunal Examinador de Médicos de Puerto Rico, se anunciare o se hiciere pasar como médico, cirujano, osteópata, o como profesional en el ejercicio de cualquiera de las profesiones auxiliares reguladas por esta ley, y que pretendiere estar capacitado para diagnosticar, tratar, operar, o recetar para cualquier enfermedad, dolor, lesión, deformidad, o condición física, o que lleve a cabo o se ofrezca por cualesquiera medios o métodos para diagnosticar, tratar, ope-

rar, o recetar para cualquier enfermedad, dolor, lesión, deformidad, o condición física, recibo o no remuneración por tales servicios. Los estudiantes de medicina debidamente matriculados en escuelas médicas organizadas en Puerto Rico podrán, bajo la supervisión docente de un médico debidamente autorizado para ejercer la medicina en Puerto Rico, llevar a cabo exámenes en seres humanos, recetar, ayudar en operaciones, dar anestesia, atender casos de cirugía menor y atender casos de parto como parte de sus estudios, mientras asisten a la escuela de medicina. Constituirán, además, delito menos grave sujeto a las mismas penalidades enumeradas anteriormente las siguientes prácticas:

“(1) El uso del título de “doctor en medicina”, o de la abreviatura M. D., usada esta sola, o asociada a otros términos, con el propósito de solicitar pacientes, excepto en los casos de personas que estuvieren legalmente autorizadas para ejercer la medicina en Puerto Rico. (2) El uso de los términos “especialista pédico”, “cirujano pédico”, “cirujano ortopédico”, “especialista ortopédico”, o cualquiera otra derivación de los mismos, si no es persona autorizada para ejercer la profesión médica en Puerto Rico. (3) El anunciarse como “quiropodista” o podiatra, a menos que sea un podiatra legalmente autorizado para ejercer dicha profesión en este Estado Libre Asociado, haciendo saber que el anunciante trata enfermedades y dolencias de las condiciones anormales de los pies.”

“Artículo 10. El Tribunal podrá ofrecer periódicamente exámenes de reválida totales o parciales en o fuera de Puerto Rico por lo menos dos veces al año y de acuerdo con normas que establezca el Tribunal Examinador en Coordinación con el Departamento de Estado.”

“Artículo 11. Los exámenes de reválida de médicos cirujanos o osteópatas se efectuarán por escrito y según las reglas que dicte el Tribunal. Dichos exámenes incluirán, pero sin limitarlos, aquellas materias sobre las ciencias básicas a la medicina y disciplinas clínicas que el Tribunal estime convenientes.”

“Los exámenes podrán ser contestados en los idiomas inglés o español, a elección del examinado.”

“Artículo 12. Los derechos de exámenes y certificados o licencias serán determinados por el Secretario de Estado. Todos los derechos se pagarán por adelantado en giro postal o cheque certificado, a nombre o a la orden del Secretario de Estado. Todo aquél que no lograse pasar el examen requerido o por causa justificada y aceptable para el Tribunal no hubiere podido presentarse a la convocatoria correspondiente, tendrá el privilegio de ser admitido a tomar el examen próximo, libre de derechos. El importe de estos derechos no

será devuelto al solicitante por dejar de presentarse a examen, ni por haber sido desaprobado. Los candidatos a examen, sólo tendrán cinco oportunidades para tomar dicho examen; requiriéndosele que demuestren haber recibido entrenamiento adicional de seis (6) meses por lo menos en una escuela de medicina u hospital reconocido por el Tribunal Examinador de Puerto Rico, para que el Tribunal, les brinde oportunidades adicionales para tomarlo.”

“Artículo 13. Todos los fondos recaudados por cualquier concepto por cada una de las juntas examinadoras y juntas de registro enumeradas en la sección 3 de este título, ingresarán al Fondo General del Tesoro Estatal.” (20 LPRA 6).

“Todos los egresos por concepto de servicios personales así como cualquier otro gasto incurrido en la realización de los propósitos para los cuales fueron creadas todas y cada una de las juntas examinadoras y juntas de registro, se pagarán de aquellas asignaciones que considere necesarias la Legislatura de Puerto Rico y que se incluirá en el Presupuesto General de Gastos.” (20 LPRA 7).

“Artículo 14. Toda persona que aspire a obtener licencia para ejercer en el Estado Libre Asociado de Puerto Rico la profesión de médico cirujano o la de osteópata, deberá cumplir con los siguientes requisitos:”

“(1) Ser mayor de edad y ciudadano de Estados Unidos de América o residir con carácter de permanencia un mínimo de tres (3) años en Puerto Rico.”

“(2) Poseer un diploma, título de médico cirujano u osteópata o certificado de haber completado satisfactoriamente todos los estudios académicos de la carrera de médico-cirujano u osteópata, expedido por alguna universidad, cuyo curso de estudios esté aceptado y registrado por el Tribunal Examinador de Médicos de Puerto Rico. El Tribunal Examinador no reconocerá la validez de un título de médico cirujano u osteópata en aquellos casos en que el aspirante no haya cursado, por lo menos, los dos últimos años de su carrera en la Escuela de Medicina que lo expide, si dicha Escuela es extranjera. Tampoco aceptará la validez de un título si la Escuela de Medicina que lo expide excusó al aspirante de tomar cualquier asignatura incluida en el currículo normal, aceptado y registrado por el Tribunal Examinador de Médicos de Puerto Rico.”

“(3) Haber aprobado los exámenes a que se refiere el artículo 11 de esta ley. El Tribunal Examinador de Médicos podrá eximir del requisito de examen a aquellas personas que hayan obtenido licencia para ejercer dicha profesión mediante exámenes aprobados

ante el tribunal correspondiente en los estados de la Unión Americana, con los cuales el Tribunal Examinador de Médicos haya establecido relaciones de reciprocidad, y a aquellos médicos cirujanos que posean un diploma expedido por el Tribunal Nacional de Examinadores Médicos (National Board of Medical Examiners of the United States of America). En ambos casos dichos médicos cirujanos deberán cumplir con los demás requisitos exigidos en este artículo.”

“(4) El aspirante suministrará evidencia satisfactoria al Tribunal Examinador de Médicos de que después de haberse graduado en la escuela de medicina ha trabajado como interno o residente por no menos de un año en un hospital aprobado por el tribunal.”

“(5) Practicar por un período mínimo de un año como médico en el servicio público de Puerto Rico en el sitio que designe el Secretario de Salud en consulta con el médico y aprobado por el Tribunal Examinador de Médicos de Puerto Rico, mediante licencia especial expedida al efecto, indicando el pueblo donde habrá de llevarse a cabo dicha práctica. Se entenderá por el “servicio público” el servicio prestado en Puerto Rico en los servicios médicos asistenciales, municipales, estatales o federales y como residentes en hospitales gubernamentales, estatales, municipales o federales y hospitales con fines no lucrativos, con programas de residencia aprobados por el Consejo de Educación Médica de la Asociación Médica Americana. Si se presentare un candidato a licencia y no hubiere vacante una posición en el servicio público, que permita al aspirante cumplir con este requisito, el Secretario de Salud así lo informará al Tribunal Examinador de Médicos y dicho Tribunal eximirá al aspirante del cumplimiento de dicho requisito. Se faculta al Tribunal Examinador de Médicos para que de común acuerdo con el Secretario de Salud, autorice a médicos con más de diez (10) años de práctica, reconocidamente especializados en los distintos campos de la medicina o médicos que a la fecha de aprobación de esta ley, hayan cumplido o estén en vías de cumplir un período de residencia especializada en un hospital de los Estados Unidos, a cumplir este requisito bajo condiciones especiales que permitan que el interés público reciba el máximo beneficio que pueda derivarse de una juiciosa y eficaz utilización por el estado, de los servicios especializados de tales médicos. Cualquier médico que no haya podido cumplir con los requisitos que dispone este inciso, por estar sirviendo como tal en las Fuerzas Armadas de los Estados Unidos, estará exento de cumplir con dichos requisitos al regresar a Puerto Rico.”

“(6) Aquellas personas que se hubieran graduado

antes de la aprobación de esta ley serán admitidos al ejercicio de la profesión al someter en lugar del requisito de un año de internado, evidencia de haber ejercido legalmente la profesión de medicina por un período de cinco años en los Estados Unidos o en cualquier otro país.”

“En el caso de médicos de buena reputación científica que vinieren al Estado Libre Asociado de Puerto Rico y desearan ejercer la medicina, el Tribunal Examinador de Médicos, podrá después de aquilatar los méritos y autoridad científica del interesado, librarle la correspondiente licencia para ejercer la medicina en Puerto Rico, por término de un año, prorrogable a discreción del Tribunal Examinador de Médicos.”

“No podrá desempeñar las funciones de médico cirujano en ningún cargo público, ninguna persona que no haya sido previamente autorizada por dicho tribunal, para ejercer la profesión de médico-cirujano en Puerto Rico. La infracción de cualquiera de estas disposiciones constituirá práctica ilegal de la medicina, con las consiguientes responsabilidades. A petición del Tribunal Examinador de Médicos, el Secretario de Justicia de Puerto Rico, solicitará un auto de Injunction para impedir que la persona acusada de ejercer ilegalmente la medicina y cirugía o sus profesiones aliadas en este Estado Libre Asociado, continúe el ejercicio de dicha profesión de médico o de cualesquiera de sus ramas, hasta tanto se resuelva la acusación.”

“Artículo 15. Los médicos del Ejército, Marina y Servicio de Sanidad Pública (United States Army and Public-Health Service), quedan dispensados de los exámenes anotados en el Artículo 11, y podrán ejercer la medicina en Puerto Rico, mientras se encuentren en el ejercicio activo de sus funciones oficiales, para lo cual deben obtener una licencia especial expedida por el Tribunal y pagar veinticinco (25) dólares de derechos además de cumplir con lo establecido en el Artículo 14 de esta Ley. Este derecho se entenderá que ha cesado tan pronto como cesara en el ejercicio de sus funciones oficiales.”

“Artículo 16. Quedan también exentos de los requisitos de examen, aquellos médicos-cirujanos que posean un diploma expedido por el Tribunal Nacional de Médicos Examinadores (National Board of Medical Examiners of the United States of America), pero deberán obtener su licencia y pagar los derechos correspondientes, según el Artículo 12.”

“Artículo 17. El Tribunal expedirá una licencia provisional especial autorizando la práctica de la medicina y cirugía en Puerto Rico, a todo médico cirujano que deseara ingresar como médico interno o residente

en cualquier hospital o clínica en Puerto Rico, antes de haber aprobado los exámenes de reválida ante el Tribunal Examinador de Médicos. Dicha licencia provisional será expedida por el término de un año, luego que las credenciales exigidas por la ley sean debidamente aprobadas. El solicitante de la licencia provisional deberá presentar al Tribunal todas las credenciales exigidas por ley para ser admitido a examen, excepto la de ciudadanía o residencia."

"La licencia provisional especial podrá renovarse anualmente por el término de dos años. Este término podrá extenderse en aquellos casos en que se trate de extranjeros que practican la medicina en cualquier institución reconocida para entrenamiento médico."

"La omisión de este requisito constituirá práctica ilegal de la medicina en Puerto Rico."

"Artículo 18. El Tribunal Examinador de Médicos estará autorizado para establecer, mediante las condiciones y requisitos que juzgue necesarios, relaciones de reciprocidad de dispensa de examen, directamente con los "Estados Unidos de América", o de cualquier otro país, cuyos Tribunales exijan el más alto grado de educación profesional; Disponiéndose, que el Tribunal Examinador de Médicos podrá conceder a los médicos que sean ciudadanos de otros países los mismos privilegios y derechos que esos países concedan a los médicos de los Estados Unidos y de Puerto Rico. En el caso de revocación de licencias por el Estado de Nueva York u otro estado en el cual el Tribunal Examinador de Médicos de Puerto Rico tenga convenio de reciprocidad, o por el National Board of Medical Examiners de los Estados Unidos, —ipsosfacto—quedará revocada también la licencia que haya sido extendida por el Tribunal Examinador de Médicos de Puerto Rico al mismo interesado."

"Artículo 19. El Tribunal Examinador de Médicos deberá llevar un registro conteniendo el nombre, número de la licencia, dirección residencial y otra información que se estime pertinente de toda persona que obtuviere una licencia de dicho Tribunal. Todo médico vendrá obligado a renovar su licencia cada cuatro (4) años, mediante el pago de diez (10) dólares."

"Artículo 20. Para el ejercicio de la profesión de enfermería obstétrica en el Estado Libre Asociado de Puerto Rico, se requerirá la obtención de una licencia, para la expedición de la cual se deberán llenar a satisfacción del Tribunal, los requisitos señalados a continuación: Ser mayor de edad, saludable física y mentalmente, de buena conducta moral y ser graduada de una escuela superior reconocida por el Departamento de Instrucción Pública del Estado Libre Asociado o su

equivalente. La identificación de las solicitantes se hará mediante declaración jurada por las mismas, y de cualesquiera otras pruebas que el Tribunal Examinador exigiere. Se exigirá a toda solicitante que presente una licencia en vigor de enfermera graduada y ser graduada de una escuela de enfermería obstétrica reconocida por el Tribunal, cuya graduación sea el producto de estudios teóricos prácticos por un período no menor de 6 meses durante los cuales las estudiantes completarán un currículo a base de práctica supervisada por la facultad médica y de enfermería obstétrica de una escuela debidamente organizada para este propósito. Esta práctica incluirá la atención de 25 alumbramientos normales y experiencia clínica en el manejo de casos en las distintas fases de la obstetricia, incluyendo la participación en el manejo de los aspectos de la obstetricia complicada. La experiencia clínica deberá efectuarse en aquellas facilidades hospitalarias que para este propósito estén debidamente reconocidas por el Tribunal Examinador de Médicos. Aceptadas las solicitantes, éstas deberán aprobar un examen teórico en obstetricia que incluya, además, los fundamentos y principios pediátricos y ginecológicos que forman parte del ciclo obstétrico. El examen se llevará a cabo de conformidad con las reglas y reglamentos que dicte el Tribunal. Aprobado el examen, el Tribunal expedirá a cada interesada una licencia autorizándola para ejercer la profesión de enfermería obstétrica en el Estado Libre Asociado de Puerto Rico; Disponiéndose, que tal licencia sólo autorizará la asistencia de partos normales; y el cuidado de la madre durante las distintas fases del ciclo materno, ambos bajo supervisión médica."

El Tribunal Examinador de Médicos reglamentará la práctica de la profesión de enfermería obstétrica. Será motivo de cancelación de la licencia la infracción a las disposiciones de los reglamentos dictados por el Tribunal Examinador de Médicos a tales efectos. La cancelación se llevará a efecto según dispone el Artículo 23 de esta Ley.

Se autoriza al Departamento de Salud para expedir, cuando lo crea conveniente, permiso de *comadrona auxiliar*; para fijar las facultades y deberes de las mismas, y para dar y fijar la instrucción a ese efecto correspondiente, sin la cual no podrá expedirse tal permiso."

"Artículo 21. Toda persona que desee ejercer la profesión de practicante en Puerto Rico deberá, al solicitar la licencia correspondiente, además de someter al Tribunal, las pruebas de su identificación personal, y los diplomas, o certificados que posea, llenar los impresos

que le sean suministrados por el Secretario de Estado y demostrar que es mayor de edad, que goza de buena salud y reputación moral. Presentará además, un certificado acreditativo de haber cursado y aprobado las materias exigidas en los dos primeros años de estudio de instrucción secundaria. Deberá poseer y presentar, asimismo, un diploma obtenido mediante tres años de estudios teóricos y prácticos en uno o varios hospitales, reconocidos por dicho Tribunal como competentes para impartir la necesaria instrucción."

"Deberán, además, tomar y aprobar examen elemental ante dicho Tribunal, de las siguientes materias: física, química, anatomía y fisiología humanas, bacteriología, terapéutica, materia farmacéutica, toxicología, patología médica y quirúrgica, higiene pública y privada, asepsia y antisepsia. Pasarán además un examen práctico sobre aplicaciones de apósitos y vendajes, curaciones y cuidado de pacientes. Ambos exámenes, el teórico y el práctico, se efectuarán de acuerdo con las reglas y reglamentos que dicte el Tribunal. Aprobados estos exámenes, el Tribunal expedirá al interesado una licencia autorizándolo para ejercer libremente la profesión de practicante en el Estado Libre Asociado de Puerto Rico; Disponiéndose, que nada de lo contenido en este Artículo referente a requisitos para ser admitido a examen, afectará a los que con anterioridad a la aprobación de la Ley de 30 de julio de 1923, sufrieron su examen y así como a aquellos que aún conservan sus solicitudes en el archivo del Tribunal Examinador de Médicos; Disponiéndose, además, que los que poseen licencias de practicantes, ejercerán su profesión tan sólo dentro de los límites que los estudios aprobados para adquirir la misma determinan, y aplicarán sus conocimientos únicamente en casos de cirugía menor, y en aquellos casos en que actúen bajo la dirección y supervisión de un médico cirujano; Disponiéndose, también, que la infracción de las anteriores disposiciones, excepto cuando se trate de primeros auxilios en casos de envenenamientos, hemorragias graves, quemaduras, heridas graves, fracturas y cualquier otro estado de urgencia, será considerado como práctica ilegal de la medicina, sujeto a la penalidad que marca el Artículo 9 de esta Ley y a las disciplinarias que señala el Artículo 14 de la misma."

"Artículo 21-A. Toda persona que aspire a obtener licencia para ejercer la profesión de podiatría en Puerto Rico deberá llenar los siguientes requisitos:"

"(1) Ser mayor de edad y residir con carácter de permanencia en los Estados Unidos de América o ser ciudadano de los Estados Unidos de América."

"(2) Haber aprobado los exámenes de reválida de podiatras que versarán, entre otras asignaturas, sobre bacteriología, histología, anatomía, patología, fisiología, química, práctica de podiatría, materia médica y terapéutica."

"(3) Poseer un diploma o título de podiatra expedido por alguna escuela de Podiatría reconocida por el Tribunal Examinador de Médicos, cuyo curso de estudios sea de no menos de cuatro (4) años luego de haber aprobado un curso de no menos de dos (2) años del currículo normal conducente a la obtención de un bachillerato en una universidad o colegio acreditado."

"Una vez llenados los requisitos anteriores, el solicitante que deseara ser admitido a examen deberá llenar los impresos que suministra el Tribunal para que se acredite bajo juramento ante Notario Público: su identidad, la autenticidad de los diplomas y títulos que posee, su mayoría de edad y los certificados de buena conducta y reputación. Una vez aprobados los exámenes que señala la cláusula (2) de este artículo, el Tribunal expedirá al interesado una licencia, autorizándolo a ejercer libremente la profesión de podiatra en el Estado Libre Asociado de Puerto Rico."

"Artículo 22. De acuerdo con lo establecido en el Artículo 10 de la ley original del año 1903, los archivos pertenecientes a la extinta sub-delegación de Medicina quedan en poder del Tribunal así como los del actual Tribunal Examinador de Médicos."

"Artículo 23. El Tribunal Examinador de Médicos, o el Secretario de Estado, por su propia iniciativa, o a virtud de queja o denuncia debidamente fundada, de cualquier persona natural o jurídica, podrá en cualquier momento investigar la identidad de cualquier persona que pretenda ser, o se anunciare o haga pasar como médico cirujano, osteópata, podiatra, practicante, enfermera obstetra o comadrona, licenciado o no, por el Tribunal y después de notificar por escrito al interesado, tendrá poder para exigirle que presente pruebas razonables y a satisfacción del Tribunal de que posee una licencia legalmente obtenida para practicar su profesión en el Estado Libre Asociado de Puerto Rico y de que en realidad es la persona a quien originalmente se expidió dicha licencia. Si de la investigación resultare que el denunciado no tiene licencia para practicar, o no le pertenece legítimamente la que posee, ésta será anulada por el Tribunal y, además, en cualquiera de los dos casos traspasará el expediente al Secretario de Justicia de Puerto Rico para la debida persecución de los in-

factores ante los tribunales del país; disponiéndose, que el Tribunal Examinador de Médicos tendrá poder para retirar y anular, temporal o definitivamente, la licencia que poseyere cualquier médico-cirujano, osteópata, podiatra, practicante, enfermera obstetra o comadrona que fuere convicto ante este Tribunal de haber incurrido en fraude o engaños cometido durante el ejercicio de la profesión, de haber cometido delito grave (felony), de ser alcohólico consuetudinario; adicto al uso de drogas narcóticas; de practicar o de ayudar a efectuar, de cualquier manera, método o forma, un aborto criminal de una mujer; de excederse en las atribuciones profesionales que le señala esta ley; de mala práctica en el ejercicio de su profesión, es decir: de incompetencia burda y manifiesta, con perjuicio de tercero; de conducta inmoral y deshonrosa; disponiéndose, asimismo, que el procedimiento a seguir para la anulación o suspensión temporal de una licencia será incoado por uno de los miembros del Tribunal designado por el Presidente, asesorado por el Secretario de Justicia de Puerto Rico, a virtud de querella presentada por cualquiera de los miembros del Tribunal o declaración jurada presentada por cualquier ciudadano. La querella o declaración deberá en todo caso aducir hechos que prima facie constituyan causa probable. El querellado tendrá para su defensa ante el Tribunal Examinador de Médicos todos los derechos concedidos a personas acusadas de delito, con excepción del juicio o investigación por jurado; disponiéndose, igualmente, que en todos los casos de anulación o suspensión de licencias el fallo del Tribunal Examinador de Médicos será comunicado a las auto-

dades fiscales y policíacas del Estado Libre Asociado para que exijan su debido cumplimiento; pero en los casos a los que se refiere el disponiéndose inmediato anterior, y siempre que el fallo fuere la anulación o suspensión de licencia por más de un año, dicho fallo no será firme ni comunicado a las autoridades fiscales y policíacas, mientras el Tribunal Superior no lo haya revisado y juzgado el caso; y la persona interesada podrá apelar para ante dicho Tribunal dentro del término de treinta días."

"Artículo 24. Toda persona que ejerciere cualquiera de las profesiones auxiliares de la medicina y cirugía en Puerto Rico sin licencia legal para ello, incurrirá en las mismas penas que determina el artículo 9 de esta ley. Disponiéndose, que dentro de los noventa días después de la aprobación de esta ley, toda persona que haya ejercido la quiropodía o podiatría en Puerto Rico por un período mayor de dieciocho (18) meses podrá solicitar por escrito una licencia del Tribunal Examinador de Médicos, quien vendrá obligado a extenderla sin examen siempre y cuando la evidencia presentada compruebe la competencia profesional del solicitante y disponiéndose que los solicitantes cubiertos bajo este artículo podrán ser, o ciudadanos de Estados Unidos, o residentes de Puerto Rico."

"Artículo 25. Toda ley o parte de la misma que se oponga a la presente, queda por ésta derogada."

"Artículo 26. Esta Ley empezará a regir a los 90 días después de su aprobación."

CARTAS A LA REDACCION

Dr. Jorge O. Just Viera
Presidente Junta Editora
Boletín Asociación Médica de Puerto Rico
Santurce, Puerto Rico 00908

Dear Dr. Just:

The following observations are submitted to you in hopes that you might publish them in a future issue of the BOLETIN.

The article entitled "Rheumatic Carditis Causing Acute Trifascicular Block", by Altieri, Johnson, Crenshaw, and García Palmieri (BOLETIN 63: 323, 1971) was very interesting. The authors demonstrate well the involvement of the anterior division of the left and right bundles. The involvement of the posterior division of the left bundle, however, is not well demonstrated.

The assumption is made that there is delayed conduction through the posterior division of the left bundle in the presence of a first-degree atrioventricular (AV) block. But at no time the authors show left axis deviation alternating with right axis deviation. If this would have been apparent in the electrocardiogram (ECG) then they could have concluded that the posterior division of the left bundle was involved (1).

It is not possible to tell from a surface ECG whether the site of delay in a first-degree AV block is in the AV node or at a site lower in the conduction system (2). In the particular case presented one could only validate the hypothesis of delayed conduction in the posterior division of the left bundle by direct recording of potentials in the bundle of His.

Francisco Jaime Anselmi, MD
Chief Cardiac Cath. Lab.
Mayaguez Medical Center

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- (2) Narula, O. S., and Samet, P.: Wencekbach and Mobitz II A-V Block Due to Block Within the His Bundle and Bundle Branches. Circulation 41: 947, 1970.

Dr. Jorge O. Just Viera
Presidente Junta Editora
Boletín Asociación Médica de P. R.
Santurce, P. R. 00908

Dear Dr. Just:

In relation to Dr. Jaime's letter of January 12, 1972, discussing some of the electrocardiographic findings of the case of trifascicular block due to rheumatic carditis (Boletín: 63: 323, 1971) I want to make the following comments:

1. I agree with him that the only way to be 100 percent sure where a block is you must do intracavitary recordings, but when there is a severe myocarditis with left ventricular dysfunction the existence of a right bundle branch (RBBB) with left anterior hemiblock (LAH) strongly suggest that the additionally affected fascicle is located at the ventricular level. Therefore it should be anticipated that in most cases of RBBB with LAH in patients with severe left ventricular dysfunction different degrees of A-V block will be related to additional involvement of the main left bundle branch or its posterior division (1).
2. It is true that recordings of His bundle potentials may help to rule out A-V node and main bundle as the site of the A-V block, but recordings from the main left bundle itself would be needed to determine whether additional block occurs at the level of the main left bundle or of the other division (2-4).
3. Not even a normal P-R interval with RBBB plus LAD in the presence of a normal A-H and H-V intervals will rule out delay conduction in the posterior division, because you must study the above intervals during atrial pacing or during spontaneous atrial premature beats (2-4).
4. Both Ranganathan and Narula studies would indicate that the findings of RBBB, LAD (LAH) and a prolonged P-R interval denote that the third site of block is commonly located in the AV node

(A-H interval lengthened and H-V interval normal), or more distally, namely the posterior fascicle of the left bundle branch (normal A-H interval with a prolonged H-V interval); perhaps both sides of block, or even others, may participate. If the block were strictly nodal, rather than in the posterior fascicle, the term, trifascicular block, of course, would not apply (2, 3).

Sincerely,

Pablo I. Altieri, MD
Division of Cardiology
Ohio State University
Columbus, Ohio

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2. Ranganathan, W., Dhurandhar, R., Philips, JH and Wingle, ED: His bundle electrogram in bundle branch block. *Circulation* 45: 282, 1972.
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COMENTARIOS A UNA CARTA PUBLICADA EN EL BOLETIN DEL MES DE ABRIL DE 1972

Satisfacción y orgullo me produjo leer la "Carta a la Redacción" escrita con elegancia, sentimiento y fervor patriótico por el distinguido colega Dr. J. Rodríguez Pastor.

Se trata de un médico puertorriqueño que realizó sus estudios profesionales en los Estados Unidos y se lamenta con razón de que prácticamente hayamos desterrado de nuestras actividades científicas el idioma que primero nos susurraron al oído nuestras madres.

En torno a ella hilvana estos pensamientos un médico cincuentenario, nacido en una aldea asturiana incrustada en Los Picos de Europa, que pasó por el Seminario en la Península y por la Universidad en la República de Cuba y que ahora ejerce la medicina en esta "Isla del Encanto".

Nuestro idioma es bello, expresivo y sentimental. Cuanto más se adentra en su estudio, más se percata de su flexibilidad y dulzura. Pero además de las

razones intrínsecas del idioma existen razones de dignidad de pueblo.

Cuando asistimos a una conferencia por un disertante de habla hispana y con un auditorio casi exclusivo de la propia lengua en el idioma inglés, lo primero que hacemos es levantarnos y salirnos del Salón de Conferencias. Porque lo estimamos una pedantería. Además en muchas ocasiones el inglés con que se expresan deja mucho que desear. No juzgado por mí que soy un lego en la materia, sino por expertos en el idioma. Está muy bien y es correcto, cortés que cuando hay visitantes extranjeros se intercalen durante la conferencia extractos y comentarios en el idioma de su país.

Los países de habla hispana y de otras nacionalidades envían a Washington o a Londres a sus representantes diplomáticos que hablen el inglés, a Francia que hablen el francés, a Alemania que hablen el alemán, etc. Eso constituye una muestra de respeto y consideración para el país donde van a convivir, que se traduce en eficacia y simpatía.

Esa actitud de nuestros asociados del Norte, hasta cierto punto despectiva para los países de América Latina les ha traído la malquerencia de los mismos. Las ayudas económicas quedan opacadas por la falta de sensibilidad. Nuestros pueblos aprecian más el espíritu que la materia.

Pude observar en la Cuba de hoy, que gira en la órbita del Imperialismo Soviético, cómo los Técnicos del bloque comunista (Rusos, Chinos, Checos, etc.) se esforzaban por aprender el idioma castellano y lo aprendían rápidamente los que no lo sabían. Le imponen a un pueblo su sistema pero no le imponen su idioma, porque el idioma es una cosa sagrada con la cual nacemos.

Está muy bien que aprendamos el inglés y más idiomas si tenemos facilidades para ello, pero sintámonos orgullosos del nuestro.

Las tres colonias que se separan de España en la Guerra Hispano-Americana presentan las siguientes características:

Cuba mantuvo y mantiene su idioma a pesar de las fuerzas opresivas foráneas y son éstas las que tienen que aprenderse el idioma de Cervantes.

Filipinas va perdiendo su idioma vernáculo. Hoy predomina el inglés en las nuevas generaciones. No es de extrañarse que algún día tengan que hablar el Japonés o el Chino. Cuando un pueblo no lucha por mantener la lengua materna se expone a estas contingencias.

Puerto Rico conserva el idioma vernáculo porque está incrustado en el corazón de sus Jíbaros. Las clases

profesionales, que generalmente son las dirigentes, tienen un deber patriótico: mantener y enaltecer su lengua vernácula, sin que esto obste para que perfeccionen el idioma de Shakespeare y estimulen el aprendizaje del idioma de nuestro Asociado del Norte.

Reciba nuestros parabienes el Dr. Rodríguez Pastor por haber alertado a nuestra clase médica sobre "la res-

ponsabilidad que le corresponde en la conservación y dignificación de nuestra cultura hispánica"

Con ello estamos dando un ejemplo de dignidad y patriotismo. Los Pueblos no se valoran por su tamaño, sino por la grandeza de su espíritu.

Dr. Ismael Rodríguez Ibañez

NOTICIAS

Del Recinto de Ciencias Médicas-Universidad de Puerto Rico:

El tercero en la serie de Cursos de Perfeccionamiento que ofrece la Escuela de Medicina para médicos del país se iniciará el primero de agosto próximo, según informó el director asociado de dicha actividad educativa.

Dijo el doctor Egidio Colón Rivera que esta vez, además de poder matricularse para el curso entero de seis meses, los candidatos pueden estudiar sólo aquellos segmentos del currículo que más les interesa. La matrícula será limitada a 50 médicos, añadió.

Entre los quince segmentos que componen el curso figuran obstetricia y ginecología, pediatría, cirugía, y diferentes áreas de medicina tales como hematología, biología celular, siquiatria y salud de la comunidad.

Según señaló el doctor y profesor Colón Rivera, el currículo total se compone de 95 conferencias dictadas por distintos profesionales, mayormente miembros de la facultad de la Escuela de Medicina del Recinto de Ciencias Médicas de la U.P.R. El curso concluye a principios de febrero de 1973.

Participarán en las demostraciones clínicas los Hospitales Universitario, de Veteranos y Municipal de San Juan. También colaboran el Departamento de Salud, la Asociación Médica de Puerto Rico, la Junta Estatal de Examinadores, y el Programa Médico Regional.

El financiamiento del curso proviene en parte del gobierno de Estados Unidos, con aportaciones por parte del Departamento de Salud y la Escuela de Medicina.

El curso también cubre nutrición, endocrinología, el riñón y balance de líquidos y electrolitos, infecciones, los sistemas cardiovascular y respiratorio, el hígado y sistema digestivo, y neurología.

Para más información — R. Norris Blake, 767-2675.

THIRTEENTH CONGRESS - PAN-PACIFIC SURGICAL ASSOCIATION — FEBRUARY 15-21, 1975 - PLACE: Hilton Hawaiian Village Hotel, Honolulu, Hawaii. **FOR DETAILS, WRITE:** César B. De Jesús, MD, Pan-Pacific Surgical Association, 236 Alexander Young Building, Honolulu, Hawaii, 96813.

From the Saratoga Drug, Inc. - Myron R. Kligerman, Reg. Ph. 690 Main Street, Springfield, Mass. 01105:

"We have an opportunity for a Spanish speaking physician (General Practitioner) to locate here. Actually the space available is large enough for two or more physicians who might

want to operate as a clinic. The office was previously occupied by a very busy doctor whose records are available, his widow has even left some of the equipment there."

"The practice is by no means Spanish speaking only, however, it is my feeling that a city of this size (200,000) with a Spanish speaking population of over 20,000 should have a doctor that understands them and can communicate with them. A doctor who wants to practice community medicine with a major Welfare clientele can earn \$40,000 to \$50,000 the first year. We shall supply the office which is air-conditioned and heated at no charge for 5 years."

From the Journal of the Indiana State Medical Association.

DARVON — A recent article published in the New England Journal of Medicine reported that the efficacy of Darvon as a pain reliever could not be substantiated by a double-blind study. The authors' conclusions are difficult to understand.

Darvon was admitted to the market as an analgesic by itself or in combination with aspirin and other analgesic drugs after full clinical trials were carried out to the satisfaction of the Food and Drug Administration. This FDA approval was reinforced by a study of another salt of propoxyphene —Darvon-NTM — a study which was continued for several years and culminated in FDA approval, at a time when the FDA is meticulous in assessment of effectiveness.

It is a common clinical observation that Darvon serves well and probably best when it is combined with other analgesic drugs and especially with aspirin. The combination of a peripherally acting substance with Darvon, which is primarily central in action, is remarkably effective.

The NAS/NRC panel commented that "the combination of Darvon with an antipyretic-analgesic of the aspirin type results in analgesia superior to that achieved by either drug administered alone.

Another mysterious development came to light when the NEJM article reported that, in one method which was used to analyze the results, 65 mg of Darvon ranked higher than 65 mg of codeine.

Darvon products have been in widespread clinical use for 15 years. As the politicians express it, "Let's look at the record". It is a record of millions of patients who have obtained satisfactory relief of mild to moderate pain from Darvon and its combinations, with an unusually high degree of safety.

From the American Hospital Association News Release:

CHICAGO — In a strongly worded letter to the Secretary

of Health, Education and Welfare, the American Hospital Association, has said the government is, in effect, putting the responsibility of providing health care for the poor on the backs of paying hospital patients.

Responding to Secretary Elliot Richardson's proposed restriction on Hill-Burton funding (that grant recipients provide free services to the poor at not less than five per cent of their total operating costs, or not less than 25 per cent of their net income), the AHA emphasized that the ability of hospitals to finance care for the poor is largely dependent on obtaining

the necessary funds from charges to other patients.

"The problems of providing health care for the poor is a responsibility of all people in the country and should not be placed on the backs of hospital patients. In effect, this proposed regulation is not only completely unfair, but it is also thoroughly misleading to the poor of the country. There is no magic about financing hospital care . . . Every dollar of care provided must be paid for," the letter, written by AHA Deputy Director Kenneth Williamson, states.

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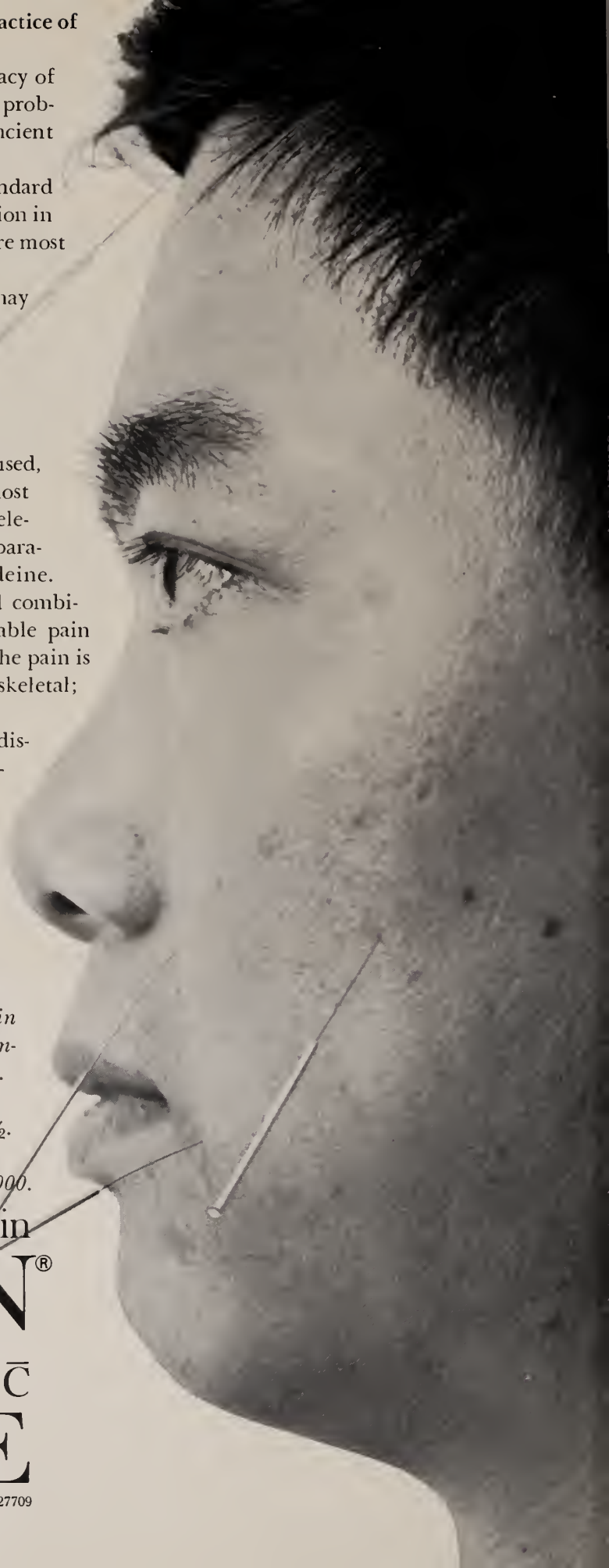
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Empirin Compound with Codeine No. 3 contains codeine phosphate (32.4 mg.) gr. 1/2. No. 4 contains codeine phosphate* (64.8 mg.) gr. 1. *(Warning—may be habit-forming.) Each tablet also contains: aspirin gr. 3 1/2, phenacetin gr. 2 1/2, caffeine gr. 1/2. Bottles of 100 and 1000.*

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Presentación: Frascos de 30 y 90

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When it's mandatory to keep the post-coronary patient calm, consider Valium (diazepam).

Although he's promised to take it easy back on the job, you know he's going back to the same stressful circumstances that may have contributed to his hospitalization. If he experiences excessive anxiety and tension because of overreaction to stress, your prescription for Valium can bring relief. During the period of readjustment Valium can quiet undue anxiety.

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The most commonly reported side effects are drowsiness, ataxia and fatigue. Until individual response is determined, caution patient against driving or operating dangerous machinery.

Valium® (diazepam) For the tense cardiac patient who must be kept calm

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures.

Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision.

Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg *b.i.d.* to *q.i.d.*; alcoholism, 10 mg *t.i.d.* or *q.i.d.* in first 24 hours, then 5 mg or *q.i.d.* as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg or *q.i.d.*; adjunctively in convulsive disorders, 2 to 10 mg *b.i.d.* to *q.i.d.* **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated (See Precautions.) **Children:** 1 to 2 mg *t.i.d.* or *q.i.d.* initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

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BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

THE DEXTROCARDIAS. (SECOND PART)	195
<i>A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects</i>	
<i>Charles D. Johnson, MD</i>	
CRYPTOCOCCUS NEOFORMANS: THEIR IDENTIFICATION IN BODY FLUIDS AND CULTURES BY MUCICARMINE STAIN (MAYER)	203
<i>J. F. López, MD and R. Figueroa Lebrón, MD</i>	
ELECTROCARDIOGRAFIA CUANTITATIVA EN LA UNIDAD DE CUIDADO CORONARIO	206
<i>F. Olazábal, Jr., MD, J. Oms, MD y R. Rodríguez, MD</i>	
POST GRADUATE MEDICINE IN PUERTO RICO	211
<i>A. Refresher Course</i>	
<i>Egidio S. Colón-Rivera, MD</i>	
NOTICIAS	218



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

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Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.



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Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

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El Boletín se publica mensualmente. Todo material de anuncio está sujeto a aprobación por la Junta Editora.

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Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

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rheumatoid arthritic blowup...

Tandearil® Geigy
oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, including those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of water. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Contraindications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Precautions: Children 14 years or less; senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; sinusitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, presence of concomitant diseases, and concurrent drug chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially to predict benefits against potential risk of severe, fatal, reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B) 98-146-800-E

For complete details, including dosage, please see full prescribing information.

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Low humidity and large pollen counts will irritate the eyes. That's why it's good to keep your eyes moist with a preservative-free artificial tear drops. It's convenient, it's safe, and it's available at the drug store. You'll feel better all day, all night, all year-round. From nose to neck, it's good for all seasons.

And it's available only on your prescription. So make sure you're using the right one.

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We're not against all her E. coli...

only the E. coli in her
urinary tract

Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. And it does not suppress normal bac-

**Basic in cystitis*, pyelitis*,
pyelonephritis***

the one-tract action of

Macrochantin® Capsules (nitrofurantoin macrocrystals) 50mg/100mg.

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, staph aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatic or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have known hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and a small percentage of ethnic groups of Mediterranean

and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur, reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

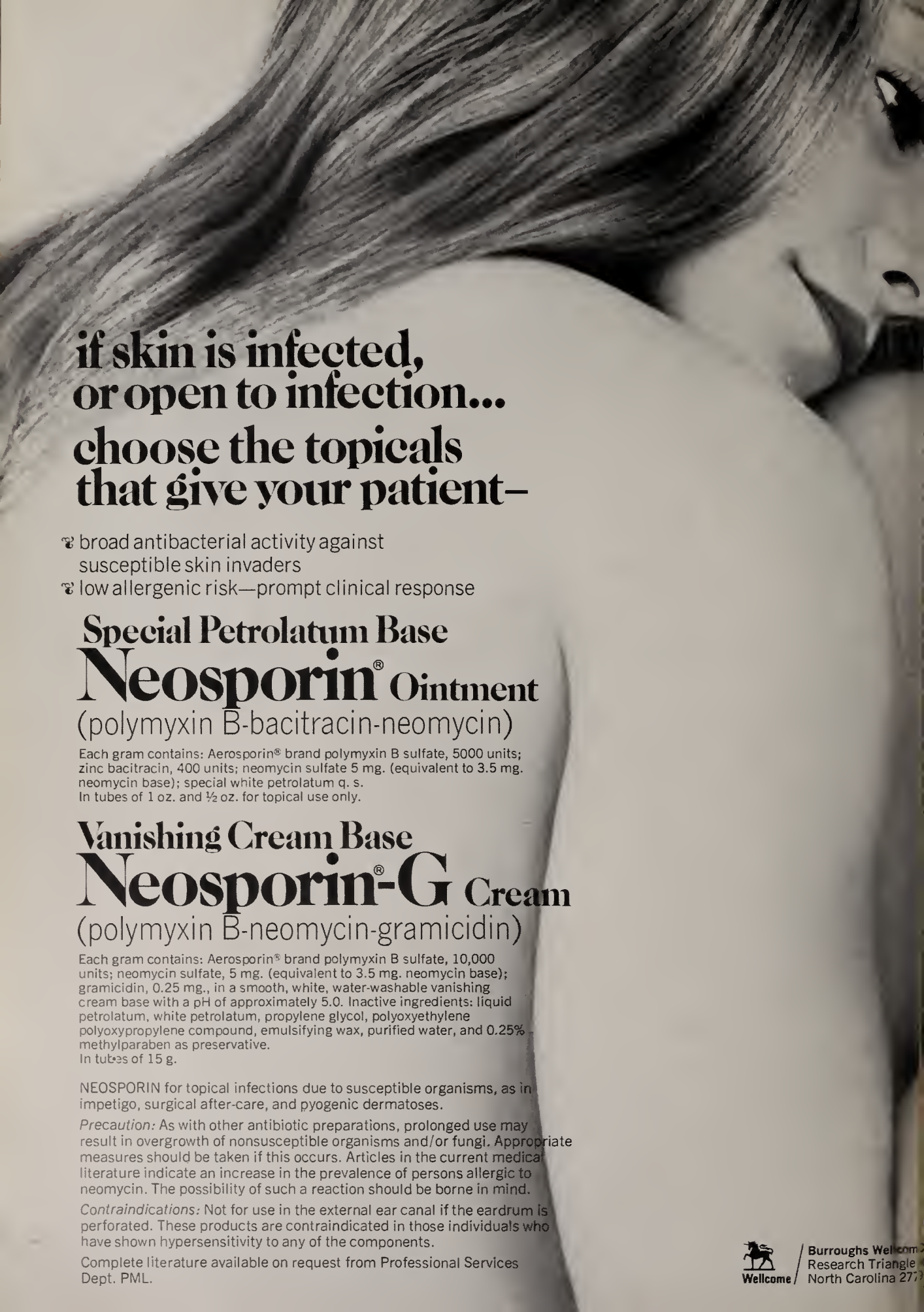
terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms.



Originators and Developers of The Nitrofurans
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or open to infection...
choose the topicals
that give your patient—**

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Neosporin[®] Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin[®] brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
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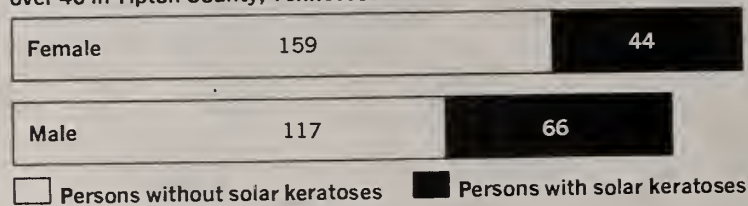
What it means to live and work in Tipton County, Tennessee

**Persons who are white and
over 40 have one chance in four
of having solar keratoses...
which may be premalignant**

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**Prevalence of solar keratoses in white persons
over 40 in Tipton County, Tennessee**



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



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*De acuerdo a un informe del American Journal of Public Health, Vol. 56, No. 56.

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THE DEXTROCARDIAS. *A Review and a Report of 26 Cases, emphasizing Electrocardiographic and Vectorcardiographic Aspects.* (SECOND PART)

Charles D. Johnson, MD

Discussion

Cardiac malpositions, including the dextrocardias, have fascinated physicians for centuries! Diagnosis may be easy, or on the other hand overlooked, to the chagrin of the examiner. The numerous and varied classifications, the nomenclature, has unduly hindered understanding. Other associated anomalies may be present with the dextrocardia, and these actually constitute the important clinical and physiological abnormalities. Following Daves and Pryor's excellent article on cardiac positions, their basic definitions will be listed (15).

	Location of Stomach Bubble and Descending Aorta
1. Normal (levocardia) = leftward apex with situs solitus (s.s.).	Left
2. Levoversion = leftward apex with situs inversus (S.I.).	Right
3. Dextrocardia = rightward apex with S.I.	Right
4. Dextroversion = rightward apex with S.S.	Left
5. Mesocardia = midline apex with S.S.	Left
6. Mesoversion = midline apex with S.I.	Right

Any of these six apex-situs alignments may exist with any of the following four internal alignments (15):

1. Normal	RA → RV → PA
2. Transposition (Tr)	RA → RV → Ao
3 (complete)	
3. Corrected Tr.	RA → LV → PA
4. Ventricular Tr.	RA → LV → Ao

The aorta (Ao) and pulmonary artery (PA) may vary in their relationship to one another, independent of their ventricular connections. There is a predictable great vessel relationship to the type of heart (15).

Transposition refers to a change in the anterior-posterior relationship of the great vessels, while inversion refers to a change (reversal) in the right-left relations of the atria, ventricles or great arteries. The position of the apex usually but not always is formed by the left ventricle (the right ventricle can uncommonly form the apex) (12, 15). Mixed dextrocardia refers to the state of the cardiac apex being rightward, but the atria and/or ventricles are not reversed (3, 4). Dextroversion has dif-

ferent meanings, but usually implies that the ventricular portion of the heart is rotated to the right, while the remaining cardiac structures, including the atria, are in their normal position (called also dextrorotation, pivotal dextrocardia, dextrotorsion, isolated dextrocardia) (4, 16). The left ventricle (LV) lies a little more anterior than normal, and anterior to the right ventricle (RV). The right atrium (RA) is to the right and slightly posterior; the left atrium (LA) lies to the left and slightly anterior; the cardiac apex may be formed by the right ventricle. The septum tends to be perpendicular to the frontal plane. Dextroposition means that the heart lies in the right hemithorax, due to extra-cardiac factors, such as atelectasis, pleural effusion, pneumothorax, obstructive emphysema, or absence of the right lung (17). "Corrected transposition" comprises transposition plus inversion of ventricles, with functional correction. Anatomically corrected transposition is another term for ventricular transposition (15). Noninverted transposition, inverted transposition and isolated ventricular inversion are terms used by Lev (4) and Shafer (11) to refer to complete transposition, corrected transposition and ventricular transposition, respectively.

Situs inversus consists of (1, 18):

- A. Concordant — L — bulboventricular loop (RV located to the left, and LV to the right). (Normal inversely related great arteries or complete transposition; l-transposition)
- B. Discordant — D — bulboventricular loop (RV located to right). (Corrected transposition; d-transposition)
- C. Indeterminate bulboventricular loop.

Simple clinical and physical examination may uncover the rightsided heart. Left-handedness (which may be present in 40 percent of patients with mirror-image dextrocardia) (19, 20), position of liver dullness and stomach tympany, and the level of the testicles (right lower than the left), should be sought. Palpation of the anterior right and left chest wall, and the presence of louder heart sounds, murmurs, and split second sound over the right chest may be helpful. In meso-

version, a strong apical impulse may be seen or felt in the xiphoid area, with little cardiac dullness. Sinusitis and bronchiectasis and dextrocardia constitute Kartagener's Syndrome; this has been found in about 25 percent of patients with dextrocardia, usually without associated cardiac malformations. Bronchiectasis is about 100 times more frequent (12-23 percent) in cases of situs inversus than normally (22). The pain of an acute myocardial infarction may be referred to the right chest and right arm in dextrocardia. There may be a reversal of the relation between the values of the electromechanical interval of the left-and-right sided precordial pulsations (23). A family history may uncover other cases of the Kartagener triad. Surgery may reveal the liver and appendix to be on the left side of the abdomen, with left abdominal appendiceal pain. Dextrocardia may first be detected by routine chest and abdominal roentgenography (24). Left and right symbols must be identified. The apex of the heart is usually projected over the lower hemidiaphragm, irrespective if it is left or right, and irrespective of the presence of anomalous positions of other organs (25). Van Mierop recently reported on the use of the tracheo-bronchial tree (air-filled trachea and main bronchi) as an indicator of visceral situs, since the situs of the atria corresponds to that of the lungs, and the situs of the atria (except for rare instances) determines the visceral situs — as seen on chest radiograms taken in the PA or AP projections (26). Contrast media will delineate the position of the stomach and colon. The RA (all chambers in terms of anatomy) is located on the same side as the liver, while the aortic arch, LA and stomach are located on the same side of the body (9, 10, 20, 27). This almost pathogemonic rule is not true when there are other rare complex, cyanotic, heart defects associated with asplenia (Ivemark's Syndrome), polysplenia, a midline liver (visceral heterotaxy, isomerism), venous anomalies, and hematological findings such as Howell-Jolly and Heinz bodies, numerous normoblasts, poikilocytosis, anisocytosis, target cells and siderotic granules in the red blood cells (1, 28). Radio-isotope scans may localize the liver and spleen or spleens (29). The position of a catheter in the venae cavae localizes the RA, and there may be difficulty in advancing the catheter beyond the RV in dextroversion and mixed dextrocardia (7). Following atrial identification, one then attempts to identify and localize the ventricles. The ECG may be of some assistance here, but it should consist of 16 leads, the usual 12 leads plus right precordial leads (30). The right and left arm lead wires may be interchanged. Additional ventricular hypertrophy and

conduction disturbances should be noted. The status of the great vessels (anterior/posterior) should then be added, along with any associated congenital heart defects. This and the anatomical ventricular identifications are best diagnosed by selective angiography (each cardiac chamber has its own peculiar anatomical features; the higher of the two semilunar valves identifies the RV). Following the van Praagh's, the logical approach would be (27):

1. Determine the type of viscerotrial situs.
 - a. X-Ray-liver, stomach
 - b. ECG
 - c. Cardiac catheterization
2. Determine the type of bulboventricular loop (relation of great arteries to ventricles).
 - a. Angiography
 - b. ECG
 - c. van Praagh's rule.
3. Then fit the loop to the viscerotrial situs, thereby assembling the heart-veins, atria, great arteries and ventricles. Note concordance or discordance of loop.
4. Then work-out any associated anomalies
ECG, cardiac catheterization, angiography.

Van Praagh's rule (5 percent exceptions may exist) says that the type of the great arteries at the semilunar valves (by angiography) indicates the type of cardiac loop, and hence the ventricular location; the morphologic RV connects with whichever of the two great arteries is the more anterior (1). Normally related great arteries and d-transposition indicate a D-bulboventricular loop with the RV being located to the right, while inversely related great arteries and l-transposition indicates an L-loop and the RV being located to the left since the RV develops from the bulbus cordis and the LV from the common ventricle. In situs inversus, if the aorta arises on the right of the pulmonary artery, a D-loop is probably present, and if on the left, an L-loop. If transposition of the great vessels is absent, discordant bulboventricular loop development is virtually excluded (18).

Several general assumptions have been found of value in diagnosis of the dextrocardias (1, 20, 30): Some authorities believe that Tetralogy of Fallot is very rare in mirror-image dextrocardia, and in cyanotic dextrocardia (others have found cyanotic lesions, such as Tetralogy of Fallot); rather, in this situation, transposition of the great arteries, a VSD and PS are thought to be present instead; if acyanotic, corrected transposition with a VSD, with or without PS. A cyanotic dextrocardia is not dextroversion; there are no known

cases of Tetralogy of Fallot in dextroversion—so in dextrocardia an upright P and a left-sided stomach practically excludes this diagnosis. “Mirrow-image” dextrocardia (P inverted and stomach on right) is believed to be the most common type of dextrocardia, especially in the cyanotic patient. “Corrected transposition” is the most common lesion, but 90-95 percent of patients with “mirrow-image” dextrocardia have normal hearts. (Other series, however, showed 53 percent with associated intracardiac lesions) (7). Mesocardia is seen frequently in the syndrome of asplenia (bilateral right-sidedness) with cyanosis, decreased pulmonary blood flow, a transverse liver and hematological abnormalities. Corrected transposition is frequent in patients with centrally placed hearts (mesoverversion) in whom the apex is difficult to define. A single ventricle (SV) occurs in about 20 percent of cases of dextrocardia and in some 50 percent of cases of mixed dextrocardia.

Dextroversion is associated with heart disease in 75-95 percent of cases, usually with cyanosis, and complex lesions such as corrected transposition, septal defects, SV, pulmonary stenosis or atresia; both of the ventricular chambers can be smoothwalled (1, 11, 20). The aortic arch is on the same side as the LA and opposite to the apex (9, 10).


Neill and Mirowski believed that if an adequate ECG did not lead to ready identification of the ventricular position, then a complex malformation associated with situs inversus or transposition was almost always present (30).

Campbell and Reynolds have stated that when the P wave of the ECG is upright in lead I, the sinoatrial (S. A.) node, and hence the RA and venae cavae, are located on the right side, and when the P wave in lead I is inverted, these are located leftward (atrial inversion) (2). A “qR” type of complex identifies the location of the LV, while an “R/S” complex denotes an underlying RV (17).

However, these potentially diagnostic indexes are not always so valuable. Arrhythmias are quite common in the dextrocardias and the polarity of the P waves is known to change frequently, and even within a single electrocardiograph lead of the same patient (30). Left atrial ectopic rhythms (LAER) have been found in several cases of mirrow-image dextrocardia, dextroversion, and normally placed malformed hearts and provide diagnostic problems, as they may cause inversion of P waves in lead I and V₆, along with “dome and dart” P waves in V₁ (31).

Junctional (including coronary sinus) rhythms, and

their differentiation from LAER's, are other diagnostic difficulties (32). The status of these arrhythmias is presently controversial. Situs indeterminus with atrial isomerism adds further dilemmas. A negative P wave in lead I may possibly be found too in marked right atrial enlargement. Also, the q wave associated with RVH may be misleading.

The ECG in the dextrocardia has been described by Portillo and associates (17), Burch and DePasquale (33), Perloff (20), Mirowski (30, 34), Neill and others (1, 2, 7, 21, 23). An rS or R/S complex is recorded more frequently over the RV than the LV; an rSR, rsR or rRS suggests the RV. The LV is identified by a qRs, qRS, qR, QRs, QR or Qr complex. Mirrow-image dextrocardia with situs inversus is characterized by: A lead I that shows inverted P and T waves, and a prominent S—, which is the mirrow-image of the situs solitus heart; lead II records the pattern of lead III, and lead III that of lead II; lead AVR records the pattern of AVL, and AVL that of AVR. (AVL shows inverted waves). The right precordial leads present the usual pattern of the left precordial leads, and lead V₁ presents the pattern of V₂, and vice versa. Since ventricular activation and repolarization are the mirrow-image of normal, Q_{II} Q_{III}, S_I S_{II}, or S_I S_{II}, S_{III} patterns may be present. An rS is present in lead V₆ while qR complexes are seen in the right lateral precordial leads; the P and T waves are negative in V₄₋₆; lead AVF is similar to the normal. Other authorities have found, however, that the P wave may be positive at some time in mirrow-image dextrocardia in perhaps approximately 50 percent of the cases.

In the presence of “dome and dart” P waves and LAER, an upright P wave in lead I suggests atrial inversion, while an inverted P wave suggests a normal atrial position.

In dextroversion, the P waves are characteristically diphasic (—+) in lead I, positive in leads II and III; but the P in lead I may be upright, low or inverted (junctional rhythm) with a progressive increase in P wave voltage from the right to the left precordial leads. Portillo and associates' early studies revealed the RV morphologies to be located more to the right than usual (rS in V₅ R, V₆ R, prominent R or R/S) with the transition near V₁ and V₃ R (R/S complexes), and prominent R waves in V₁₋₂. Left ventricular activity was recorded more to the right, in leads V₁ to V₃, as qR complexes; the R waves become smaller from leads V₃ to V₆, and appear as qR or more likely qr in V₆. Lead V₆ R is similar to V₁ of the situs solitus heart, while V₂ is similar to lead V₆. Left ventricular activity faces the left but more anterior

than normally, as RV activity faces the right, but more posterior than usual. A qr or QR is present in lead I; deep Q waves may be present in leads II and III, with R or S waves. Leads AVR, AVL and AVF may show rS, QR, or qR patterns, respectively. In uncomplicated dextroversion the mean electrical axis is inferiorly and slightly to the right or left. The T axis is inferior and to the right (or left), negative in leads I, AVL, low or isoelectric in V_{3-6} , and positive in leads III, AVR, V_{1-2} , and V_3R to V_6R (17, 20, 33).

In mirror-image dextrocardia, RBBB was manifested as a late wide R (QR) wave in lead I and an RR' or rR' configuration in the right precordial leads, and without late S waves in lead I and the left precordial leads; lead V_1 and V_2 may show rSR complex and a negative T wave, lead V_4R an R/S and V_6R a qRs complex with a positive T wave (35). With LBBB there may be a QS complex with a positive T wave over the RV up to lead V_4R and a broad notched R wave with a negative T in V_6R . This (LBBB) suggests dextrocardia of a complex type and is relatively common in a cyanotic patient with corrected transposition (30). With RVH, there may be predominant R waves in lead I, with a qR in I, AVL, dominant R in II, AVF; tall R in V_6 , R/S in V_6R ; in LVH there is a prominent S in V_1 and a prominent R in V_6R or only a negative P in lead I. In dextroversion, RVH manifests with a right axis, prominent deep Q waves in lead I, prominent R waves in leads III, AVF, V_5R and V_6R and prominent S waves in leads I, AVR, V_{4-6} , while LVH manifests as a superior and left axis, prominent R waves in leads I, AVL, V_1 , V_2 , V_3R , a qR complex in leads V_3 to V_6 , prominent S waves in leads III, AVR and V_6R , and septal q waves in the precordial leads. Corrected transposition causes a reversal of the expected precordial q pattern, irrespective of the basic cardiac position (20, 23, 30). Shem-Tov and associates found uniform features in dextroversion and corrected transposition: (a) a Q wave in leads I, II, AVL and the left precordial leads; (b) an RS or rS wave in lead AVR; and (c) a negative T wave in AVL (23). If the P waves suggest atrial inversion and the liver shadow is symmetrical and the stomach is abnormal for situs inversus (central or left-sided), the diagnosis is probably asplenia and not situs inversus (30); the P waves are variable in asplenia hearts. In dextroposition the ECG is normal or similar to that of dextroversion, except for low voltage if pleural effusion or pneumothorax are present (17).

The electrocardiographic hint of an abnormal plane

to the ventricular septum may be the clue to a highly complex malformation (30).

As early as 1959, Portillo and associates found the ECG to provide definite aid in the diagnosis of the dextrocardias (17). On the other hand, vectorcardiographic reports are few and these consist of the cube system of electrode placement. In 1963, Sangiorgi and associates studied seven cases of mirror-image dextrocardia, employing the Grishman cube system (14). In the following year Bilger and colleagues studied twelve patients with mirror-image dextrocardia, also with the cube system (14).

Gasul and associates described the clinical features, the ECG and VCG in 47 cases of dextrocardia (7). Their findings added to the previously detailed information. Right atrial enlargement in mirror-image dextrocardia caused tall, peaked P waves in leads II, III and AVF, while left atrial enlargement shifted the P axis to the right, superiorly and posteriorly (negative P waves in leads I, II, III, AVL, AVF, and left precordial leads), and made the P waves broad and notched. There were no specific findings in the mixed dextrocardias, and the location of the ventricles was difficult to determine using the morphologic QRS patterns.

The vectorcardiogram in mirror-image dextrocardia revealed a clockwise P loop (F, H planes) oriented to the right, inferiorly and slightly anteriorly. The QRS loops were oriented to the right, inferiorly and slightly posteriorly, rotating clockwise in the horizontal plane, and either clockwise or counterclockwise in the frontal plane; the initial part of the loop was to the left and anteriorly. Right ventricular hypertrophy tended to reverse the horizontal inscription of the loop and oriented it anteriorly, inferiorly and to the left. In dextroversion, the P loop was located anteriorly, inferiorly and slightly to the left; with RVH, the QRS loops were located to the right, superiorly and slightly anteriorly, rotating counterclockwise in the frontal plane, and either counterclockwise or figure-eight in the horizontal plane. The vectorcardiogram in mesoversion demonstrated narrow and vertical QRS loops in the horizontal and frontal planes, and a clockwise broad loop in the sagittal plane (7).

Clockwise rotation of the P loop in a frontal plane VCG (1 case of mirror-image dextrocardia) was shown in 3 cases to be a distinctive and critical sign of dextrocardia, provided the P wave originated from the sinus node (Frank system). The frontal plane P loop in a normally situated heart travels in a counterclockwise direction. The mean frontal plane axis of each of the P loops was about $+90^\circ$. These

authors believed that this finding excluded dextro-position of the heart and hypertrophy of the right heart from chronic lung diseases (36).

The frontal plane in mirror-image dextrocardia is a mirror image of the normal.

A counterclockwise F. plane loop suggests a complex type of dextrocardia, such as the splenic agenesis heart with an AV canal defect.

Cardiac arrhythmias occur not infrequently in the dextrocardias and situs inversus; these consist of ectopic atrial rhythms, junctional and coronary sinus rhythms. Hastreiter and Rodríguez-Coronel described 3 patients with an anomalous inferior vena cava with azygous continuation, a high sinus venosus ASD, alterations in sinoatrial rhythm (LAER, sinus standstill with nodal escapes), a counterclockwise loop in the frontal plane, and mild cardiac and visceral heterotaxia (37). Momma and Linde analyzed the P waves and cardiac arrhythmias of 40 patients with dextrocardia (38). In mirror-image dextrocardia the P waves were rightward ($+120^{\circ}$ to $+150^{\circ}$ in F plane) in most cases—P waves inverted in lead I and V_6 , upright in leads II, III and in the right chest leads, including V_6R ; whereas the P vector in dextroversion was vertically downward ($+80^{\circ}$ to $+100^{\circ}$) in about one third of the cases—flat or $+d$ biphasic in lead I, and in the normal range ($+15^{\circ}$ to $+75^{\circ}$)—upright in leads I, II, III, V_{2-6} —in the majority. Left atrial rhythms were associated with bilateral superior venae cavae, and coronary sinus rhythm occurred with the polysplenia syndrome or absent inferior vena cavae (IVC), ASD or VSD. Coronary sinus rhythms in patients with dextroversion were highly suggestive of an absent IVC, partial situs inversus and possibly associated complex cardiac anomalies. A F plane P wave axis between $+80^{\circ}$ and $+100^{\circ}$, a small negative wave followed by a small positive wave in lead II, or a positive wave followed by a negative wave in the right chest leads in a case of dextrocardia with congenital heart disease suggests dextroversion rather than mirror-image dextrocardia. The P waves in asplenia varied but typically were flat in lead I and upright in leads II and III (39). Bilateral sinoatrial nodal tissue, as found histologically by Van Mierop, may explain this (40).

Varying degrees of atrioventricular block may occur in dextrocardia with corrected transposition.

The best vectorcardiographic study is that of Miller, Medrano and Sodi-Pallares, in 1968 (14). These authors studied 17 patients (20 VCG's) with the usual cube, and inverted-cube system of electrode placement. They believed that the VCG was a useful tool in the investigation of cardiac malpositions. They described and characterized their material as: mirror-image dextrocardia

(14 studies), dextroversion (4 studies) and rotated dextroposition (2 studies). Also, they noted the presence of ventricular hypertrophy and ventricular inversion, with and without cardiopathy. A spectrum of loop configurations were depicted.

The electrocardiographic and vectorcardiographic findings in simple mirror-image dextrocardia in this study were similar to those previously noted. The initial forces were directed to the left and anteriorly, the major H QRS forces were directed to the right (posteriorly in Case 4), and the terminal forces lay in the midline or slightly to the left, as in the study of Miller and associates (14). These authors found that clockwise rotating, rightward P and T loops were also characteristic. The usual cube system of electrode placement revealed exaggeration of the H QRS forces along the anteroposterior axis due to a proximity effect, suggesting RVH, which was clarified and normalized by the inverted cube system of electrode placement. It is known that the Frank H. plane loop is usually larger and more posteriorly located than that of the cube system. Reversal of leads in Case 4 showed no change other than that of reversal of the H and F loops. Terminal forces were directed to the left, anteriorly and superiorly in the case with RBBB. Left ventricular hypertrophy produced larger loops directed to the right, and anteriorly. Reversal of leads in Case II produced, however, a posteriorly located H. plane loop and a change in the RS loop configuration. Right ventricular hypertrophy in mirror-image dextrocardia showed the H and F plane forces directed mainly to the left; the early vectors were left and anteriorly directed in Miller et al's study (14) but to the right and anterior in this study in Cases 14, 15 and 16, who were believed to have RVH. In mirror-image dextrocardia with corrected transposition (mixed dextrocardia with atrial inversion) the QRS forces were directed to the right; rightward and anterior forces were found in two of the three cases in this study. The P and QRS loops in uncomplicated dextroversion and rotated dextroposition were not strikingly different from the normal except for prominent forces directed to the left, anteriorly and inferiorly (14). But with associated LVH, the cube showed a late loop of clockwise rotation in the H plane oriented to the left and posteriorly. When corrected transposition was associated with dextroversion, the QRS loops were oriented to the right, with clockwise H rotation; the early vector was directed anteriorly and slightly to the right. The P loops were to the left and anteriorly, or anteriorly, and rotated counterclockwise in the H and F planes; the T loops were right and anteriorly directed (14). In Case 23

(Figure 15), the initial vector was to the left and anterior, with the major portions of the loop being located leftward, posteriorly and superiorly. There was predominantly counterclockwise rotation in the H and F planes. There was early and afferent slowing. The P loop was to the left and inferior, while the T loop was located also to the right and anteriorly, and inferiorly.

In levoverion the apex of the heart fails to swing to the right, but remains on the left, with the atria and abdominal viscera retaining the basic situs inversus position (this is the mirror-image of situs solitus with dextroversion) (9, 10). The RV forms the left-sided apex, the liver is on the left and the aortic arch-stomach bubble on the right (20). Complex cyanotic anomalies of the heart are almost constantly present, such as corrected transposition of the great vessels (ventricular inversion with transposition) (41). Levoverion is rare; if unaccompanied by inversion of the ventricles, it has been referred to as "mixed levocardia with atrial inversion" (7). Transposition of the great arteries (d-) and probably ventricular inversion were present in Case 26 of this series. The ECG is the mirror-image of dextroversion; lead I has an initial R wave and upright T, while q waves are absent in the left and present in the right precordial leads (20). But ventricular inversion may alter this pattern. The P waves should be inverted in leads I and V₆ and upright in AVR and V₆R. The ECG and VCG usually show a right axis deviation and RVH. The QRS loops in Case 26 were located mainly to the left, inferiorly and posteriorly.

Kartagener's syndrome has been present in about 20 percent of adults with mirror-image dextrocardia (7). It was present in one patient of this series; however, three of the patients had bronchial asthma, and six had sinusitis or some type of sinus abnormality.

Splenic agenesis ("bilateral right-sidedness") and polysplenia ("bilateral left-sidedness") may be associated with certain types of cardiovascular anomalies and extra-cardiac abnormalities (28, 42). Case 24 demonstrated the interesting syndrome of polysplenia, atrial isomerism, pulmonary and systemic venous anomalies, a mid-line liver, and anomalies of the lungs and liver.

Two basic hearts exist, situs solitus and situs inversus (10). From this, there are four basic heart positions, according to Edwards' concept:

- (1) situs solitus — atria and abdominal viscera in normal position; cardiac apex on the left.
- (2) situs solitus with dextroversion — atria and abdominal viscera in normal position; cardiac apex on the right.

- (3) situs inversus — atria and viscera in normal mirror-image position; cardiac apex on the right.
- (4) situs inversus with levoverion — atria and viscera in normal mirror-image position; cardiac apex on the left.

Addendum

Just recently, Fixler reported the first case of corrected transposition with atrial inversion and normal hemodynamics in an asymptomatic 10 years old boy with dextrocardia and situs inversus (D-loop, d-transposition) (47). The electrocardiogram revealed a P wave vector directed to the right and inferiorly (negative P waves in leads I, AVL and V₆). There were Q waves in leads V₄₋₆ and a pure R wave in V₆R. These findings indicated atrial inversion and noninverted ventricles. This case would be classified in the above nomenclature as Mixed Dextrocardia with Atrial Inversion.

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CRYPTOCOCCUS NEOFORMANS: THEIR IDENTIFICATION IN BODY FLUIDS AND CULTURES BY MUCICARMINE STAIN (MAYER)

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Mucicarmine stain has been used for many years for the detection and identification of *Cryptococcus neoformans* in tissue sections. Of all the known pathogenic fungi to man, only *C. neoformans* and *Rhinosporidium seeberi* are known to be stained by mucicarmine. The fact that they both take the stain is of no practical significance because their morphology is so dissimilar. Other commonly encountered human pathogenic fungi such as *Histoplasma capsulatum* and *Blastomyces dermatitidis* are stained by mucicarmine so infrequently and so slightly that they can be readily distinguished from *C. neoformans* (1). We wish to report our experience using the mucicarmine stain of body fluids and cultures in the detection and identification of cryptococci. Two cases of proven cryptococcosis were available for the study: case 1 had meningitis with possible cultures obtained from cerebrospinal fluid. Pathogenicity was confirmed by intracerebral inoculation to mice. Case 2 had a lobectomy for pulmonary cryptococcosis with positive sputum cultures and two cryptococcomas of the right breast removed by surgical excision. She did not develop meningitis during the time of study. Both cases were undergoing treatment with amphotericin B at the time the study was conducted.

Materials and Methods

Mucicarmine stain was performed as described by Mayer (2). Since this technique is designed for "any well fixed tissue" and "paraffin blocks" these steps were, of course, omitted. Step number one of the staining procedure was also omitted for the same reasons stated above. All smears, except those prepared from venous blood, were air dried, fixed for two hours in absolute methanol and then stained for two hours. The smears prepared from venous blood were air dried and stained for two hours without fixation. All smears were examined microscopically at 100X and 460X magnifications.

Peripheral blood: Smears obtained by venipuncture of both cases of cryptococcosis were prepared as thin smears and "buffy

coats". Control smears were prepared after suspending one loopful of a positive culture for cryptococcus (from an inoculated mouse to induce capsular formation) in 10 ml. of venous blood obtained from a healthy individual. All smears were stained with Wright's, Gomori's Methenamine-silver Nitrate (Grocott's modification) (2) and Mayer's Mucicarmine stains.

Cerebrospinal fluid: Cerebrospinal fluid from both cases of cryptococcus infections were obtained by lumbar puncture. Smears for mucicarmine stain were prepared as described above, "directly" and from sediments after centrifugation at 3,000 rpm. for 10 minutes. India ink preparations, as "wet mounts", were also examined directly and from the sediments.

Sputum: Sputum was obtained from one of the cases (case 2). Direct smears were prepared without digestion. Gram's and mucicarmine stains were utilized. Besides, smears were similarly examined of a mixture of a loopful of a positive culture for cryptococcus with a specimen of a sputum submitted for routine bacteriology to the laboratory.

Cultures: Mucicarmine stain was utilized in the study of smears prepared from a pure culture of cryptococcus, a pure culture of *Candida albicans* and a mixture of the two cultures referred to above.

Results

Peripheral blood: Smears, thin and of buffy coat, of both cases, failed to reveal any fungal elements. Smears, thin and of buffy coats, prepared from a suspension of a positive culture for cryptococcus (inoculated into a mouse) in 10 ml of peripheral blood from a healthy individual, showed a few cryptococci in the Wright's stain which were very difficult to identify. With the Gomori's methenamine-silver nitrate (Grocott's modification) the fungal elements were easily identifiable. However, they were not as prominent as the smears stained with Mayer's mucicarmine stain where the fungi could be detected even at 100X magnification (Fig. 1).

Cerebrospinal fluid: On case 2 the cerebrospinal fluid examination failed to reveal cryptococcus by any method utilized. On the other case (case 1) wet mount preparations examined with India ink show no fungus on the direct examination, and only 1 cryptococcus in the examination of the centrifuged specimen. Smears stained with Mayer's mucicarmine stain showed no fungi in the direct examination and as many as 6

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Fig. 1: *Cryptococci* in peripheral blood (buffy coat smear). Organism on top still incompletely separated from parent organism. Mucicarmine stain X460.



Fig. 2: *Cryptococcus* in spinal fluid (centrifuged sediment). Notice the single budding. Mucicarmine stain X460.

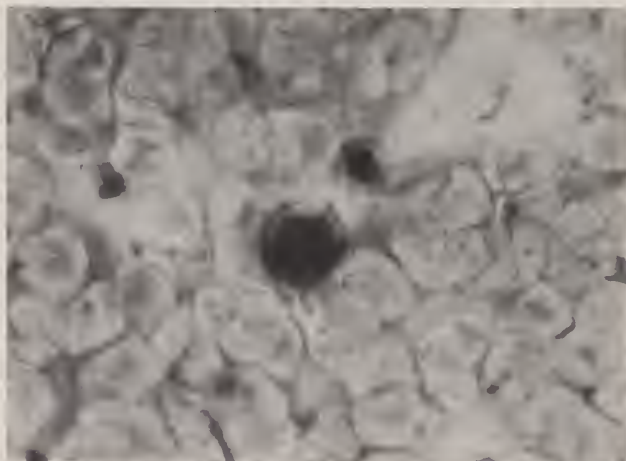


Fig. 3: *Cryptococcus* in sputum. Notice flat squamous epithelial cell above and clump of bacteria below the organism. Mucicarmine stain X460.

cryptococci per slide in the examination of the centrifuged specimen (Fig. 2).

Sputum: Smears from case 2 show numerous cryptococci deeply stained with Mayer's mucicarmine (Fig. 3). The average count was 4 organisms per slide examined. Those smears stained with Gram's stain failed to reveal the fungus. Smears of a mixture of a positive cryptococcus culture with a sputum submitted for routine bacteriology demonstrated again the cryptococci deeply stained with mucicarmine.

Cultures: *Cryptococcus* were stained with mucicarmine in smears prepared from positive pure culture and in the mixed culture. *Candida albicans* failed to take the stain whether in pure culture or in the mixed culture.

Discussion

The results of the study make evident that cryptococci can be easily found and identified by their morphology in peripheral blood, cerebrospinal fluid and sputum. The stain has not been utilized, to our knowledge, before in these body fluids. Cryptococci have never been demonstrated in blood, although it has been cultured from it. We were unable to demonstrate fungemia in our cases, but if cryptococemia was present it might have been demonstrated as shown in our control smears. The classical method of India ink preparation of cerebrospinal fluid is tedious to examine due to their "wet" nature and dry out rather quickly. The mucicarmine stained smears are permanent and, therefore, easier to study and might yield a greater number of organisms. In our second case the smears of sputum stained with mucicarmine revealed cryptococci easily while the Gram's stain failed to reveal organisms. The stain is considered useful in the examination of cultures of mucoid yeast colonies especially if a mixed flora is suspected. In the many smears examined no other fungi, epithelial cells, bacteria, leukocytes, erythrocytes, plasma or other elements stained red with the mucicarmine stain. Occasional amorphous precipitates of the stain were present which did not interfere with the examination. The stain is, in our opinion, highly recommendable for the detection and morphological identification of *Cryptococcus neoformans* in blood, cerebrospinal fluid, sputum and in the study of fungal cultures.

Summary

The authors studied smears of peripheral blood,

cerebrospinal fluid, and sputum of two cases of cryptococcosis stained with mucicarmine (Mayer). Pure cultures of cryptococci and *Candida albicans* and a mixture of both were also stained and examined. Cryptococci were easily demonstrated in smears of the cerebrospinal fluid and sputum and in those of pure culture and mixed culture. Cryptococemia was not demonstrated in the actual cases, but control smears revealed the organisms with ease. No other elements stained red with mucicarmine stain or interfere with the examination. The mucicarmine stain appears, therefore, extremely useful in the detection and morphological identification of cryptococci in body fluids and in the study of fungal cultures.

Resumen

Los autores estudiaron laminillas de sangre periférica, líquido céfalo-raquídeo y esputo de dos casos de criptocosis, así como cultivos puros y mixtos de *Cryptococcus neoformans* y *Candida albicans*. La tinción utilizada fue la de mucicarmina (Mayer). Los

criptococos fueron fácilmente demostrados en las preparaciones de líquido céfalo-raquídeo, esputos y cultivos puros y mixtos. Aunque no se encontraron criptococos en la sangre de los pacientes, sí se demostraron con facilidad en las preparaciones de control de la tinción. Los criptococos fueron los únicos elementos que se tiñeron de rojo con mucicarmina y no se observó ninguna interferencia en las laminillas examinadas. La tinción de mucicarmina nos parece extremadamente útil en la detección e identificación morfológica del criptococo en los humores corporales y en el estudio de cultivos micológicos.

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VECTOCARDIOGRAFIA CUANTITATIVA EN LA UNIDAD DE CUIDADO CORONARIO

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In 1970, los autores McConahay, McCallister, Hallerman and Smith (1), compararon el análisis cuantitativo del electrocardiograma (ECG) y el vectocardiograma (VCG) con resultados de arteriografías de las arterias coronarias. En su estudio de 210 pacientes, ellos encontraron que según iba en aumento la severidad de la enfermedad arteriográfica eran más frecuentes las manifestaciones de infarto del miocardio definitivo en el electrocardiograma y vectocardiograma. También encontraron que se le podía diagnosticar infarto del miocardio a un mayor número de pacientes con el VCG que con el ECG, y que el VCG era mejor para demostrar múltiples áreas de infarto. Si se excluían pacientes con cardiomiopatías, todos los infartos diagnosticados por VCG y todos, excepto uno, de los infartos diagnosticados por ECG estuvieron asociados con enfermedad arteriográfica significativa en la distribución arterial predicha. Ellos concluyeron que el análisis cuantitativo vectocardiográfico aparentemente era superior al análisis electrocardiográfico común en la detección de infartos pero que, cuando se podía diagnosticar infarto del miocardio, ya fuera por VCG o por ECG, se podía anticipar que habría enfermedad coronaria significativa y en una distribución anatómica predecible.

Al enterarnos de este estudio hace poco más de un año, nos pareció que ya que nos era técnicamente imposible obtener estudios arteriográficos adecuados de las coronarias en nuestros pacientes, el análisis cuantitativo del VCG prometía ser una modalidad adicional de evaluar pacientes ingresados a la Unidad de Cuidado Coronario (UCC). Si en verdad el VCG era más sensitivo para detectar infartos que el ECG, entonces contaríamos con un parámetro adicional para establecer este diagnóstico en nuestros pacientes con confianza.

Material y Métodos

Desde agosto, 1970, obtuvimos un vectocardiograma y un electrocardiograma simultáneo en todos los pacientes ingresados en la Unidad de Cuidado Coronario del Hospital Municipal de San Juan en los cuales se sospechaba un infarto del miocardio. Hasta el 22 de enero de 1971, un período de aproximadamente cinco meses, se obtuvieron un total de 107 VCGs en 101 pacientes. A 97 pacientes se les tomó un VCG a cada uno, tres pacientes se ingresaron dos veces a la unidad y cada vez se les hizo un VCG, y a un paciente ingresado cuatro veces se le hicieron cuatro VCGs.

Los VCGs se obtuvieron poco después de haberse ingresado el paciente a la unidad. Como el tratamiento de emergencia tenía prioridad, cuatro pacientes murieron sin haberse tomado el VCG. Los VCGs se tomaron con la técnica de Frank con las derivaciones torácicas a la altura del cuarto espacio intercostal cuando el paciente estaba acostado y a la altura del quinto espacio intercostal con el paciente sentado. Utilizamos dos canales electrocardiográficos de una grabadora oscilográfica de ocho canales de Electronics for Medicine conectados electrónicamente para obtener los vectocardiogramas. Los retratos se obtenían directamente del oscilógrafo de rayos catódicos y una vez revelado el papel, se montaban para su interpretación sistemática y cuantitativa en los tres planos: Frontal, Sagital derecho y horizontal utilizando varias magnificaciones cuidadosamente calibradas. Se preparó una forma especial y manualmente se determinó el ángulo y voltaje de los vectores del asa QRS a los 10, 20, 40 y 60 mseg. así como del vector máximo del asa QRS. También se midieron los voltajes y ángulos de dirección de las asas ST-T, y P. Se midió el tiempo total de duración del asa QRS y se describieron la configuración, orientación e inscripción de sus componentes, (en otras palabras: los vectores iniciales, la rama centrífuga, la rama centrípeta y y los vectores terminales). Así también, se describieron las asas ST-T y P. Cuando se llenaban los criterios diagnósticos en un plano, así se indicaba. También se copiaban las asas en la forma especial y una vez obtenida toda la data indicada se establecía un diagnóstico final.

Una vez terminados los estudios vectocardiográficos, se revisaron todos los expedientes clínicos. Usando los criterios establecidos y publicados anteriormente (2) y sin saber previamente los resultados de los VCGs, se analizó la evolución clínica y se estableció un diagnóstico clínico, estudios enzimáticos y electrocardiogramas seriados. También se investigó la evolución de la enfermedad y se obtuvieron resultados de autopsias u otros estudios subsiguientes.

Los criterios utilizados para establecer el diagnóstico vectocardiográfico de infarto, están basados en los usados por McConahay et al, quienes a su vez utilizaron criterios reciente-

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Con la asistencia técnica de la Sra. Mercedes Fernández.

TABLA I

Infarto anteroseptal — Ausencia de vectores iniciales anteriores QRS con desplazamiento posterior o hacia la izquierda del vector a los 20 mseg.
Infarto anterior — Vectores septales preservados con desplazamiento posterior del vector de 20 mseg. y de la rama centrífuga (en ausencia de hipertrofia ventricular izquierda o bloqueo completo de la rama izquierda).
Infarto anterolateral — Desplazamiento hacia la derecha del vector QRS de 20 mseg. y hacia la derecha y posterior de la rama centrífuga con vectores iniciales dirigidos hacia la derecha por más de 22 mseg. y con amplitud de 0.16 mv. o más.
Infarto lateral — Desplazamiento inferior y a la derecha de los vectores QRS iniciales, y de la rama centrífuga con inscripción horaria en el plano frontal a pesar de un vector máximo QRS mayor de $+40^{\circ}$.
Infarto inferior — En el plano frontal los vectores inferiores iniciales deben tener inscripción horaria, con una duración de 20 mseg. o más y medir más de 0.25 mv.
Infarto posterior — Debe llenar los siguientes criterios: (1) Voltaje anterior QRS de más de 0.5 mv.; (2) Tiempo de desarrollo de fuerzas máximas anteriores mayor de 30 mseg.; (3) Fuerzas máximas anteriores mayores que fuerzas posteriores; (4) Duración total de fuerzas anteriores mayor de 42 mseg.; (5) Desplazamiento anterior de la rama centrípeta en el plano transversal.

TABLA II

Diagnósticos Vectocardiográficos	Número
Infartos solitarios	52
Infartos múltiples	23
Bloqueos, rama derecha	10
Bloqueos, rama izquierda	8
Hipertrofia, ventrículo izquierdo	10
Abnormalidades 1° del asa ST-T	10
Eloqueo, división anterior superior rama fascicular izquierda	7
Bloqueo, división inferior rama fascicular izquierda	1
Bloqueo peri infarto	8
Bloqueo intra infarto	2
Hipertrofia auricular	2
Hipertrofia, ventrículo derecho	3
Marcapasos	2
Síndrome de Wolff-Parkinson-White	1

TABLA IV

Clasificación	Número
Infartos definitivos	36
Infartos probables	21
Infartos posibles	27
Misceláneo	8
Muertes	9
Autopsias	8
Arteriografías de Coronarias	1

mente publicados por Chou y Helm (3), Lamberg, Castellanos y otros. Estos criterios están resumidos en forma sencilla en la Tabla I.

Los infartos múltiples mostraban, naturalmente, una combinación de estos criterios.

Resultados

TABLA III: INFARTOS DEL MIOCARDIO

Tipos	Total	Sencillo	Múltiple
Anteroseptal	28	15	13
Anterolateral	11	5	6
Lateral	5	2	3
Inferior	43	23	20
Posterior	11	4	7
Anterior	1	1	0

La Tabla II nos muestra los diagnósticos establecidos en 101 vectocardiogramas. La Tabla III nos muestra los diagnósticos de infarto del miocardio establecidos por su localización. Sabemos por el estudio de McConahay *et al* que los infartos anteroseptales estarán asociados con hallazgos arteriográficos significativos en la arteria coronaria anterior descendente, y los inferiores con enfermedad de la coronaria derecha cuando ésta es la coronaria dominante.

La Tabla IV nos resume el resultado del análisis

de los expedientes médicos. El número de infartos definitivos fue de 36 en 92 expedientes — una incidencia mayor a la informada de otros centros. Esto se debe, seguramente, al proceso de selección que precede el ingreso del paciente a la Unidad. Hubo una perfecta correlación entre los hallazgos de autopsia y los diagnósticos establecidos excepto en una paciente con cambios solamente de ST-T que murió dos meses más tarde y en quien se descubrieron infartos anterolaterales, uno cicatrizado y el otro de origen reciente.

Presentación de Casos

Primer Caso (VCG No. 39)

Paciente del sexo femenino de cuarenta y cinco años de edad con historial de hipertensión y probable angina de pecho que fue ingresada en la Unidad de Cuidado Coronario con una taquicardia supraventricular la cual convirtió con tratamiento a ritmo sinusal. Determinaciones de enzimas séricas y electrocardiogramas seriados fueron normales. El electrocardiograma y vectocardiograma fueron normales (Figura Núm. 1).

Segundo Caso (VCG No. 101)

Paciente del sexo masculino de 58 años de edad quien fue ingresado en la UCC con el cuadro clínico de un infarto agudo del miocardio con cambios electrocardiográficos clásicos de infarto inferior agudo. Las enzimas séricas (transaminasa oxaloacética, pirúvica y la deshidrogenasa láctica) se elevaron. Clínicamente se hizo el diagnóstico de infarto agudo definitivo. El VCG demuestra un infarto inferior agudo (Figura Núm. 2).

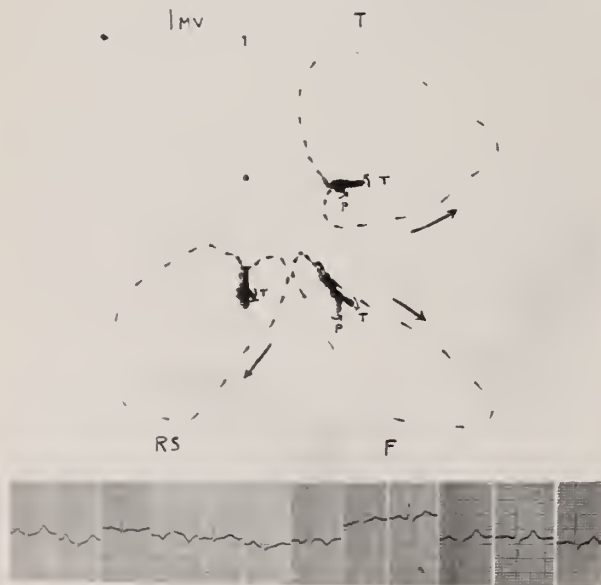


Figura 1: Vectocardiograma (VCG) y electrocardiograma (ECG) normales. Caso número uno.



Figura 2: Caso número dos - VCG y ECG revelan infarto agudo inferior.



Figura 3: Caso número tres - VCG y ECG revelan infarto anteroseptal.

Tercer Caso (VCG No. 7)

Paciente varón de 61 años de edad con historial de hipertensión, diabetes mellitus y angina de pecho, ingresado con un cuadro clínico de infarto agudo. Las enzimas séricas se elevaron y el ECG demostró infarto anteroseptal agudo. El VCG demuestra un infarto aterosseptal (Figura Núm. 3).

Cuarto Caso (VCG No. 77)

Paciente varón de 63 años de edad con un historial pasado de infarto del miocardio, ingresado a la UCC con un cuadro clásico de infarto agudo. Los niveles de transaminasa oxaloacética y la deshidrogenasa láctica se elevaron. Los ECG revelaron un infarto inferior viejo y uno anterolateral agudo. El VCG reveló un infarto inferior y uno anterior agudo con vectores septales preservados. Hay un defecto terminal de conducción de tipo peri-infarto (Figura Núm. 4).

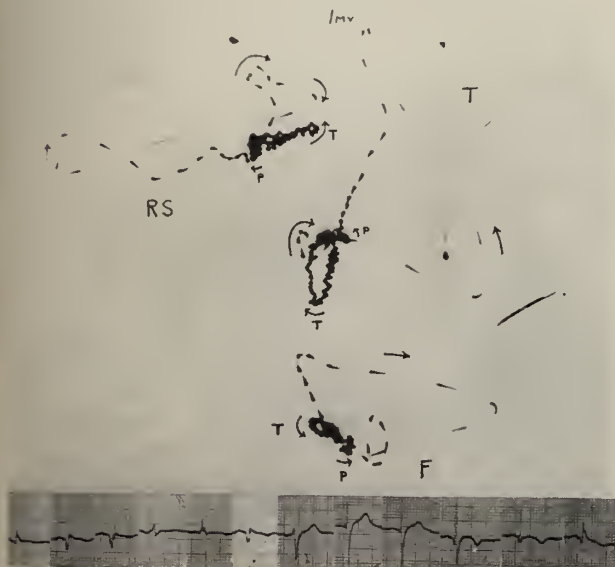


Figura 4: Caso número cuatro — VCG y ECG revelan infartos múltiples (inferior y anterolateral).

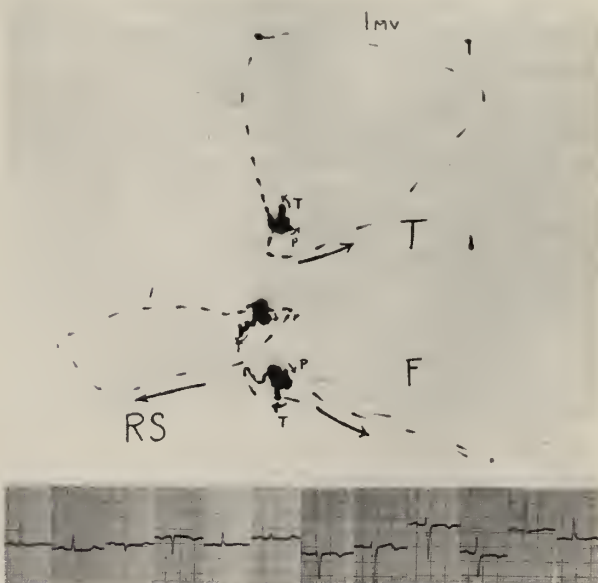
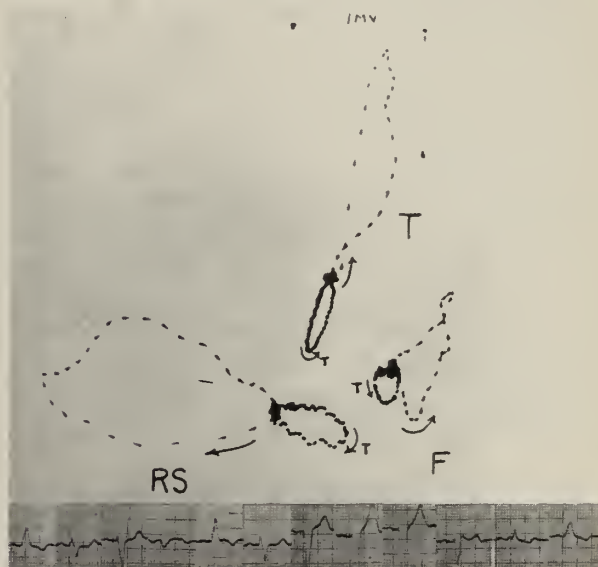
Quinto Caso (VCGs Nos. 72 y 78)

Paciente varón, médico, de 54 años de edad, fue ingresado a la UCC con un bloqueo completo de la rama fascicular izquierda y un cuadro clínico de angina de pecho. Las enzimas séricas se mantuvieron en niveles normales. El paciente fue reingresado a la UCC más tarde con un cuadro clínico similar, pero el electrocardiograma ahora reveló ausencia del bloqueo de la rama fascicular izquierda. Los VCGs (Figuras Nos. 5 y 6) mostraron inicialmente bloqueo de la rama fascicular izquierda con vectores iniciales de izquierda hacia la derecha y subsiguientemente conducción normal del asa QRS y solo cambios menores del asa ST-T. Arteriografía de las arterias coronarias hecha en el Cleveland Clinic reveló enfermedad significativa difusa sin área definitiva de infarto.

Discusión

La localización electrocardiográfica en infarto del miocardio tiene una excelente correlación con hallazgos anatómicos en autopsia y con estudios arteriográficos. El vectocardiograma, especialmente cuando se usan criterios diagnósticos cuantitativos modernos, posee

también un alto índice de certeza diagnóstica. Sin embargo, el VCG cuenta con algunas ventajas sobre el ECG. Siendo el oscilógrafo de rayos catódicos un instrumento sin problemas mecánicos de fricción, cuenta con una repuesta a frecuencias más amplias que el electrocardiógrafo. En otras palabras, es de más alta fidelidad. Esto permite la demostración de bloques intra-infartos y bloques peri-infartos en forma



Figuras 5 y 6: Caso número cinco — Bloqueo completo de la rama fascicular izquierda inicialmente que revirtieron a asa QRS normal con cambios menores del asa ST-T.

mucho más clara. En algunos de nuestros casos el médico reconocía estos hallazgos en el ECG sólo después de haber interpretado el VCG. A veces no aparecían los cambios en el ECG estando presentes éstos en el VCG. Como la manera de mostrar la actividad eléctrica del corazón también varía entre el VCG y el ECG, el VCG es ocasionalmente diagnóstico cuando el ECG es normal o sólo presenta cambios no específicos. El reciente artículo de Levine *et al* (5) muestra varios ejemplos donde el VCG es diagnóstico de infarto y el ECG permanece normal. Esto ocurre tanto en infartos inferiores así como en anterosetales y anteriores.

En infartos múltiples los cambios vectocardiográficos resultan ser a menudo mucho más impresionantes que los cambios electrocardiográficos. Usando criterios cuantitativos se pueden diagnosticar infartos múltiples cuando éstos no se reconocen en el ECG. Esta situación ocurre con una frecuencia mayor con infartos inferiores antiguos que desarrollan uno anterior agudo. Con el electrocardiograma se necesitan tener los trazados anteriores para poder establecer el diagnóstico de infarto inferior. De no tenerlos el clínico no puede establecer el diagnóstico a base de los electrocardiogramas actuales donde aparece el infarto anterior. No obstante, el VCG en estos casos suele ser diagnóstico de infarto múltiple mostrando tanto el infarto inferior así como el anterior. Esto es posible ya que los infartos inferiores se manifiestan principalmente en los planos frontal y sagital derecho sin cambios mayores en el plano horizontal mientras que los infartos anteriores se manifiestan principalmente en el plano horizontal sin haber cambios mayores en los otros dos planos.

Fue interesante observar, durante el transecurso del estudio aquí descrito, como cardiólogos expertos en la interpretación de electrocardiogramas mejoraban su lectura electrocardiográfica al contar con un vectocardiograma simultáneo. La interpretación simultánea de ECG y VCG es de gran valor ya que estos métodos son complementarios. Esta interpretación simultánea es también de gran valor educativo a residentes y "fellows" rotando por una Unidad de Cuidado Coronario.

Finalmente, los criterios cuantitativos establecidos para la interpretación del VCG y su correlación arteriográfica permite establecer clínicamente (1, 5) la localización de las lesiones arteriales. En ausencia de estudios arteriográficos adecuados, la vectocardiografía le facilita al clínico una técnica no invasiva para establecer el diagnóstico anatómicamente tanto en la localización del área interesada como en oclusión arterial específica que el paciente tendrá en la gran mayoría de los casos.

Resumen

El análisis de 107 vectocardiogramas (VCGs) tomados a 101 pacientes ingresados a una Unidad de Cuidado Coronario (UCC) bajo sospecha de haber desarrollado un infarto agudo, reveló una estrecha correlación entre el diagnóstico establecido clínicamente con el uso de electrocardiogramas (ECGs) seriados y el diagnóstico vectocardiográfico. Los VCGs mostraron un mayor número de bloqueos intra y peri-infartos que el ECG y parece ser más sensible para diagnosticar infartos múltiples. El uso del VCG en una Unidad de Cuidado Coronario agudiza la habilidad diagnóstica aún de personas expertas en la interpretación de ECGs, y es de gran valor educativo para residentes y enfermeras de la Unidad.

Summary

The analysis of 107 vectocardiograms (VCGs) taken on 101 patients admitted to a Coronary Care Unit (CCU) with the admitting diagnosis of acute myocardial infarction, revealed a high degree of correlation between the clinical diagnosis established with the use of serial electrocardiograms (ECG) and the vectocardiographic diagnosis. The VCG's demonstrated a greater number of intra and peri-infarction blocks and appeared to be more sensitive in the diagnosis of multiple infarcts. The use of VCG at a CCU sharpens the diagnostic acumen of even expert electrocardiographers and is of great educational value to residents and nurses at the unit.

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POST GRADUATE MEDICINE IN PUERTO RICO (*A Refresher Course*)

Egidio S. Colón Rivera, MD

The need for post graduate medical education for practicing physicians has been recognized by all concerned with the profession of medicine in Puerto Rico. The Medical Science Campus in general, and more specifically the School of Medicine, its Dean and faculty, as well as the Department of Health and the Board of Medical Examiners, have long been concerned about effective continuing education. Regional Medical Programs also emphasize the need for such education. The Puerto Rico Medical Association, as the formal organization representing the practitioner, has likewise placed the need for continuing medical education high on its list of priorities. In brief, all those seriously concerned with quality medical care in Puerto Rico are on record as being in favor of some means, or mechanism, for formal post graduate medical education to keep physicians current regarding medical knowledge and practices.

While all concerned agree on the necessity for providing educational opportunities, not everyone is aware of the seriousness of the situation of some graduates of foreign medical schools who repeatedly fail to qualify for a license to practice medicine. Since many of these applicants fail to pass the E.C.F.M.G. examination as well as the Puerto Rico Medical Board Examination it becomes impossible for these physicians to obtain a full and unrestricted license to practice medicine and to enter approved internships and residency programs. Sporadic efforts have been made in the past at the University District Hospital, the San Juan City Hospital and at the Ponce District Hospital to

develop courses for these physicians with some degree of success, but adequately financed, continually evaluated and periodically available learning experiences of good caliber have not been available to this group of physicians who most likely need them most. This unfortunate set of circumstances has been of deep concern to the administrators and faculty of the School of Medicine as illustrated by the following summary of past events describing efforts made to solve the problem.

Historical Background

In a meeting on March 4, 1965, the Committee on Administration of the Medical School recognized the need for post graduate medical education as one of the most serious impediments to increasing the effectiveness of health care delivery in Puerto Rico. It was decided that the School should take the initiative in determining the type of educational measures which could be undertaken in the future to help unqualified physicians. On March 23, 1965 Dr. Adán Nigaglioni, Dean of the Medical School, named an Ad hoc committee to carry out a comprehensive study of the problem and to make recommendations for its solution. Dr. Antonio Ortíz presided over this committee composed of: Dr. Manuel A. De Jesús; Dr. Francisco Ramos Morales; Dr. Angel Alberto Colón; Dr. Walter Stiehl; Dr. Américo Pomaes Lebrón; Dr. Lorenzo Galindo.

In June 1965 Dr. Antonio Ortíz presented a set of recommendations to this committee which served as a basis for the formal recommendations which came out of committee on July 9, 1965.

On September 6, 1966, Dr. José E. Sifontes, the then new Dean of the Medical School, in one of his first acts of office reactivated the previously mentioned committee. In a letter to Dr. Antonio Ortíz which presented a detailed discussion of the problem and formulated excellent objectives, the Dean created a standing committee composed of the following persons: Dr. Antonio Ortíz, President; Dr. Cristino Colón; Dr. Carlos Náter; Dr. Francisco Oliveras; Dr. Walter

Presented at the Annual Meeting of the Puerto Rico Medical Association, on November 6, 1971.

The study reported here was supported by Contract No. HSM-110-69-405, sponsored by the National Center for Health Services Research and Development, U. S. Department of Health, Education and Welfare.

Egidio S. Colón-Rivera, MD, Assistant Project Director and Associate Clinical Professor of Pediatrics.

José E. Sifontes, MD, Project Director, Professor of Pediatrics and Ex-Dean of the School of Medicine.

Stiehl; Dr. Manuel de Jesús; Dr. Juan Figueroa Longo; Dr. Francisco Ramos Morales.

Dr. Antonio Ortiz again prepared a comprehensive curriculum proposal. The committee responded by developing more definite recommendations. These included a general outline of the course, a tentative curriculum, administrative details of the course and a tentative budget. The recommendations were made in 1966. Unfortunately these recommendations could not be implemented at this time due to the fact that no funds were available neither from local sources nor from the federal government or private foundations.

Contract with the National Center for Health Services, Research and Development

During 1968, and in response to the continuous efforts of Dr. José E. Sifontes to implement a post graduate course, the Manpower Utilization Branch, National Center for Health Services Research and Development, Department of Health, Education and Welfare, demonstrated interest in carrying out a project similar to the one previously mentioned. Subsequently Miss Ida Brugnetti, Educational Consultant for the Manpower Utilization Branch, came to Puerto Rico where she, Dr. José E. Sifontes, and the Committee on Continuing Education of the School of Medicine developed a contract for the School of Medicine, Medical Sciences Campus to conduct a "Curso de Perfeccionamiento". Before entering into the contract the dean sought and obtained assurances of cooperation from the Secretary of Health of Puerto Rico, the President of the Puerto Rico Medical Association, the President of the Puerto Rico Board of Medical Examiners and the participating institutions of the Puerto Rico Medical Center.

The effective date of the contract was specified as June 27, 1969 and the expiration date was specified as June 27, 1971. (This latter date was subsequently changed to July 31, 1972). The amount of the contract was set at \$495,000 and in accordance with the conditions of the contract, the School of Medicine specifically agreed to accomplish the following:

- a. conduct a survey of eligible candidates.
- b. establish and evaluate a program of study aimed at upgrading the quality of medical education of graduates of foreign medical schools.
- c. train such graduates to provide a better quality of medicine.
- d. become more qualified to help with community health problems.
- e. be prepared to pass the State Board Examinations.

In performance of this contract, the Contractor specifically agreed to:

1. Develop a list of physicians residing in Puerto Rico who have failed the licensure examination in the past ten (10) years indicating: address, dates of examination, and the scores each achieved in the different sections of their respective examination.

2. Develop, pre-test, and administer a mail questionnaire to obtain pertinent data as to their background, education and social characteristics, present employment, experience, and attitudes toward, interest in, and availability for pursuing a special course of study aimed at upgrading their knowledge and practice of medicine and community health.

3. Assess the findings to determine the feasibility and method of measuring the level of medical and community health knowledge among those physicians interested in pursuing the course of study.

4. Develop, pre-test, and administer, to interested candidates, a brief screening method of assessing verbal and mathematical reasoning ability, English reading comprehension, and (if deemed practical) level of medical and community health knowledge so as to decide whether a course of instruction is feasible for upgrading physicians' medical and community health knowledge and skills to the desired level.

5. Based upon the results of the evaluation:

- a. Develop selection criteria for admitting candidates to the first course of instruction.
- b. Develop procedures to provide data in depth regarding the gaps and weaknesses in the candidates' level of medical and community health knowledge to serve as a guide for the curriculum for the course.

6. Select candidates based on test results, background information, scholastic record and other criteria shown to be relevant or significant.

7. Organize a special division in the School of Medicine, staffed with appropriate and sufficient personnel to implement the course of instruction.

8. Appoint a Project Director and an Assistant Project Director to carry out the program.

9. Provide training in modern methods of medical education for the participating faculty.

10. Establish a course of study with a curriculum which will be tailored to the particular needs of the physicians to be trained. Physicians selected shall be subject to approval of the Project Officer.

11. Evaluate the effectiveness of the selection procedure, the efficacy of the teaching methods and course

content by observation of instruction and periodic evaluation of the progress of the "students".

12. During the first course, the Contractor shall begin to develop procedures and techniques for providing a continuing evaluation and refinement of future courses, and recommendations to the Project Officer of refinements required.

13. Develop and implement a plan to evaluate "alumni" post-training performance in their work situations.

14. Conduct an evaluation of the impact of the first two courses on the level of Knowledge and Licensure Examination.

Implementation of the Contract

To implement the above provisions of the contract, work was initiated in the following areas:

1. Administration:

Dr. José E. Sifontes was named as Project Director, to be in charge of the overall supervision of the project, and Dr. Egidio S. Colón-Rivera was named as Assistant Project Director, to be in charge of the day to day management of the project. Dr. Francisco Veray was named Program Coordinator, in charge of the areas under the Department of Medicine, and Dr. Ariel Díaz was named Program Coordinator, in charge of the other areas covered by the course. Dr. Díaz had the additional responsibility of helping to implement the course. The Department of Psychiatry of the School of Medicine, with permission of the Secretary of Health, made space available in one of the state Psychiatric Hospital buildings where adequate offices and teaching rooms were prepared, supplies and equipment were requisitioned, and a secretarial staff of four persons plus an Administrative Assistant were employed.

A sub contract was signed with the Educational Testing Service (ETS) of Princeton, New Jersey, to help us in implementing certain features of the contract.

2. Listing of Physicians:

A list of physicians who had failed their licensure examination in the past ten (10) years was prepared by ETS and the project staff. This list included names, addresses, dates of examinations, and the scores on different sections of their respective examinations. From this list an "Educational Profile" of the group was created to determine educational deficiencies. This information was particularly useful in the final formulation of the course.

3. Questionnaires:

Two survey questionnaires were developed in cooperation with Educational Testing Services: one for physicians and another for spouses. These were mailed to some 257 physicians in December, 1969 with 139 (54 percent) of the physicians responding. Of these respondents, 104 stated a definite interest in retraining, 27 a probable interest, and 8 stated no interest at all.

A profile on the potential candidates was developed from completed questionnaires: 87 percent were males between 30 and 40 yrs. old, most were married. Those who were married had an average of 5.2 dependents. Approximately one third were from Cuba, one third from Santo Domingo and one third from Puerto Rico. Almost half (41 percent) were citizens of the United States. They grew up in cities of approximately 50,000 inhabitants and were members of comfortable, well-to-do families. The fathers of candidates tended to be small business owners or managers.

From their self-reports of academic records, 60 percent appeared to be in the top quarter of their high school classes, 50 percent in the top quarter of their college classes and 56 percent in the top quarter of their class in medical school.

About 90 percent had completed an internship. Approximately 50 percent also had received some residency training. The majority of the respondents preferred to practice in a government hospital and most considered an income of \$21,000 to \$25,000 a sign of success. The majority were willing to pursue a course of three to six months duration but stated they needed financial assistance. However they expressed a willingness to sign an agreement to work in areas of critical health need in Puerto Rico in exchange for such assistance.

They also expressed their preference for a course in basic comprehensive medicine with a focus on practice rather than on theory.

One hundred and three (103) spouses answered the questionnaires and, of these, only seven (7) did not support the idea of retraining. Most were motivated by the desire to improve their spouses status as a physician.

4. Testing Battery:

A brief screening method for assessing verbal and mathematical reasoning ability and for English reading comprehension was provided by the Educational Testing Service (E.T.S.) and consisted of the "Scholastic Aptitude Test for Predicting Graduate Work" and the "Test of English Reading Comprehen-

sion".

A "U.P.R. Medical Knowledge Test" was expressly developed for measuring the level of medical and community health knowledge of these subjects. Only the whole hearted cooperation of the faculty of the School of Medicine made possible the development of this test. This test concentrated on twelve (12) areas: six (6) on basic sciences and six (6) on clinical sciences. Two faculty members from the departments of the School of Medicine were assigned to cover each subject area. Basic techniques on how to write an adequate multiple-choice examination were presented in a two-day workshop sponsored jointly by E.T.S. and the School of Medicine. Originally eighty (80) questions were created for each subject area. Afterwards, each group met with personnel from E.T.S. and (after correcting the English and Spanish versions), they selected the sixty (60) most promising questions. These were subsequently pretested in the departments concerned and finally forty (40) questions were selected and edited for incorporation in the "UPR Medical Knowledge Test."

5. Curriculum:

The curriculum was based on the recommendations that were made by the Committee on Continuing Education.

All planning of the curriculum was done with the knowledge and cooperation of Heads of Departments of the School of Medicine. Usually they nominated to the dean a representative of their department to participate in the preparation of the actual curriculum or in some cases the Departments' Heads themselves assumed this responsibility.

The curriculum recommended was of five months duration. It began with a one week introductory period devoted to Cellular Biology and Developmental Biology, followed by study of the different body systems in blocks of one to three weeks. The basic sciences and the clinical aspects of each system were combined. Time was also assigned to areas which could not be grouped within the body systems (mostly Ob. & Gyn, Regional Surgery and certain Specialties.)

Comprehensive Medical Clinics for the practice of Family Medicine were designed for Saturday mornings and were fully supervised by a group of Internists, Pediatricians and General Practitioners. "On the spot" consultations with senior residents from the most common specialties were the high point of this block of instruction. In elaborating this curriculum the fact was stressed that the facul-

ties of the Basic and Clinical Sciences departments should be brought together so that subjects could be taught in an integrated manner. Emphasis was placed on theory as well as practice. It was also made clear that all concerned should be involved in teaching efforts. This included the faculties and other personnel of the Medical School, the University Hospital, the San Juan Municipal Hospital, the Veterans Administration Hospital and physicians in private practice. The response from all these groups was excellent and the success of the course was due to their combined efforts.

The key persons in implementing the curriculum were the coordinators who personally accepted responsibility for one of the main jobs required by the contract.

In April 1970 Dr. William Sodeinan, Consultant in Curriculum Planning at the request of the UPR, visited here for the specific purpose of evaluating the accomplishment up to that time. Following his timely and productive visit, he forwarded his report which provided a thorough analysis of a number of problems that had been identified. These recommendations were incorporated in the final curriculum.

6. Selection of Candidates:

Miss Virginia Martínez of the Section of Biostatistics of the UPR Medical Sciences Campus, School of Public Health, produced a list of candidates based on their percentile ratings on both the licensure examinations and the UPR battery of tests. Candidates were ranked in the order of their performance scores. Each candidate completed an application form and each was screened by two interviewers. Applicants' nationality, age, background information and other general criteria were also taken into consideration. With this information in hand forty eight candidates were selected according to various factors such as expectations that they would be able to complete the course successfully, their willingness to participate and the feasibility of their being released from commitments with the Department of Health.

Courses Given

On July 1, 1970, the first course started as scheduled with Students registration following the generally accepted procedures of the Medical School. On the second day they were given a medical examination including history, physical examination and routine laboratory tests. The third day was devoted to an orientation

TABLE I: FIRST CURSO DE PERFECCIONAMIENTO
July — December 1970

	U. S. A. Citizen	Foreign with 4-yr. Graduation	Foreign without 4-yr. Graduation	Total
Enrolled First Course	17	30	3	50
Completed First Course	17	27	3	47
Acquired Citizenship during Course	---	4	---	4
Took the December 1970 State Board Examination	21	23	0	44
Passed	10	17	---	27
Failed	11	6	---	17
TOTAL	21	23	---	44
LICENSE: Regular *	10	0	---	10
Provisional **	6	0	---	6
Special ***	0	17	---	17
TOTAL	16	17	---	33
Took the March 1971 Board Examination	2	1	1	4
Passed	2	0	1	3
Failed	0	1	0	1
TOTAL	2	1	1	4
LICENSE: Regular *	2	0	0	2
Provisional **	0	0	0	0
Special ***	0	0	1	1
TOTAL	2	0	1	3
Summary of licensure after both State Boards				
Regular *	12	0	0	12
Provisional **	4	0	0	4
(I+II) Special ***	0	17	1	18
TOTAL	16	17	1	34 (69 Percent)

- * Represents Permanent License
 ** License limited to one year (comparable to temporary license in U. S. A.)
 *** License awarded for 5 year period with practice limited to a government facility.

which included instruction by Mr. Belén Trujillo, the local representative of the Educational Testing Service. He provided an orientation on how to study effectively, along with a detailed explanation of the management of the multiple-choice type of examination. The course proceeded as planned and all coordinators did an excep-

tionally fine job of supervising their respective areas. The course ended the first week of December, 1970. The course graduates took the P. R. Medical Board Examination on December 10, 11 and 12. A second course started on March 1, 1971 and differed from the first one in that it was extended by approximately

TABLE II: SECOND CURSO DE PERFECCIONAMIENTO
March – August 1971

	U. S. A. Citizen	Foreign	Total	Percent
Enrolled Second Course	12	22	34	
Completed Second Course	11	21	32	
Took the September 1971 State Board Examination	11	20	31	100
Passed	6	12	18	58
Failed	5	8	13	42
LICENSE: Regular	6	—	6	19
Special	—	12	12	38
Sub-Total	6	12	18	58
Provisional	5	—	5	16
TOTAL	11	12	23	74

two weeks. This was done so that the length of the "working week" could be calculated in terms of five-day working periods. This adjustment also allowed for two extra teaching days in Surgery, Obstetrics and Gynecology, and Psychiatry. Psychiatry was scheduled earlier in the course so that students could get to know and understand themselves and each other better. Community Health was also given earlier in the course so that knowledge gained could be utilized during the rest of the course.

This second group was also introduced to the use of the "Problem Oriented Medical Record" based on a "check mark" type of record utilized in the Saturday Morning Clinics. Miss Erna Jantzen, a Medical Records consultant from the Washington Office of the Public Health Service assisted in introducing this innovation.

The second course ended on August 31, 1971 and most of the physician students took the P. R. Medical Board Examination on September 16, 17 and 18.

Evaluation

Evaluation of this endeavor was divided into two main areas: 1) evaluation of the course and 2) evaluation of the student's performance.

Evaluation of the course was completed by means

of a questionnaire prepared by Dr. J. A. Davis of the Educational Testing Service. One part of the questionnaire was filled out at the completion of each subject area and another part of the questionnaire was filled out upon completion of the entire course. The educational impact of the course was also measured by the means of pre-tests and post-tests given in each subject area. The pre-testing for each subject area was administered one or two weeks in advance of scheduled classes so that the results of each test could be made available to course coordinators. This aided in the design of the actual teaching program.

The evaluation of the student's performance was accomplished by means of pre and post testing in each area, an examination at the end of the first half of the course, and an additional examination upon completion of the second half of the course. The overall effectiveness of the course was evaluated by comparing the results of the UPR Medical Knowledge Test and the P. R. Medical Board Examination, before taking the course and after having finished it.

Dr. Antonio Bonnet, director of the Division of Medical Instrumentation of the UPR School of Medicine, was of invaluable help in the area of examination scoring. He developed a computer program which provided an item analysis of all examinations and helped deter-

mine the development of an excellent pool of examination questions. He also provided us with a detailed analysis of examination results.

Results

In general we are gratified by the results of the two courses that have been offered. Both groups showed a great deal of interest in the instruction they received. There is little doubt that being able to pass the State Board Examination was a very strong motivational factor.

The critical question, which everyone naturally asks is, "How well did course graduates do on State Board Examinations"? The complexities of licensing in Puerto Rico do not allow for a single answer to this question, therefore the results must be based upon different types of licenses which were extended by the State Board on the basis of the results of the examinations. This information is shown in Table I for the participants of the first group, and in Table II for the participants of the second group.

In the first course, twelve (12) U. S. Citizens received a Regular License, and four (4) received a Provisional License. Of the Foreign physicians, eighteen (18) obtained a Special License. This makes up a total of thirty four (34) physicians which were given a license to practice, which is sixty nine (69) percent of the total group.

In the second course six (6) U. S. Citizens obtained a Regular License, and five (5) a Provisional License. Of the foreign physicians, twelve (12) obtained a Special License. This gives a total of twenty three (23) physicians which obtained a license to practice, which is seventy four (74) percent of the total group.

A second important question concerns the professional activities in which those who have completed the courses are engaged. Up to the present time most have been assigned to an area of critical health needs. Some are in directive positions and some are working as specialists. Others have continued studying in a residency program. Their follow-up will be the subject of another study which has been sub-contracted to Educational Testing Service.

Finally, the impact of the course on the level of the actual practice of medicine is the most difficult task to measure. However, some work has already been done in developing adequate measurement criteria. Work was started at a work-shop which took place at the Hotel Barranquitas. A second sub-contract is being developed to finish this work.

Federal funds for the original two courses have been exhausted, but the hope exists that, as a result of the proven usefulness of the courses, the University, through the Medical Science Campus will be able to provide sustained financing to offer a course each year starting in June of 1972. On the basis of such a plan these courses might evolve into permanent continuing education activities available either in its totality or in parts to a wide range of physicians not necessarily foreign trained, and perhaps to students attending foreign Medical Schools who might find them useful. In addition it is expected that additional federal funds might become available for experiments in medical education leading to enhancing, at a low cost, the quality and quantity of physician manpower.

Summary

During the past two years a Refresher Course in General Medicine has been given by the School of Medicine under a contract between the Department of Health, Education and Welfare, and the Medical Science Campus. The historical background, the nature of the contract and the way it was implemented have been discussed. The evaluation and the results in the two courses given were also covered.

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NOTICIAS

From the American College of Physicians — POST GRADUATE COURSES:

- 1) "Basic Mechanisms in Internal Medicine" Sept. 25-29, 1972, Richmond, Va. The course will be held at the Medical College of Virginia, Division of Health Sciences.
- 2) "Developmental Biology and Perinatal Medicine" Oct. 2-4, 1972, in Montreal, Que., Can. The course will be held at the McGill University, Faculty of Medicine.
- 3) "Current Concepts in Hematology" Oct. 2-4, 1972, Pittsburgh School of Medicine.
- 4) "The Non-Medical Use of Drugs: Challenge to the Physician" Oct. 2-6, 1972, Newark, N. J. The course, conducted in association with the College of Medicine and Dentistry of New Jersey, will be held at the Gateway Downtowner Hotel.

For Information and Registration: Edward C. Rosenow, Jr., M. D., Executive Vice President, American College of Physicians, 4200 Pine Street, Philadelphia, Pa. 19104.

The 57th Annual Scientific Assembly of Interstate Postgraduate Medical Assn. will be held at the Washington-Hilton Hotel, Washington, D. C., November 13-16. This program, primarily designed for Family Physicians and Internists is an educational service providing a diversified lecture program, "live" Television, medical motion pictures and panel discussions.

The meeting is open to any licensed MD in the U. S. or Canada. The fee is \$25 for 26 hours of instruction, which provides credit for members of the American Academy of Family Practice who attend.

Those interested in further details and registration forms should write to Alton Ochsner, M.D., Program Chairman, Interstate Postgraduate Medical Assn., P. O. Box 5445, Madison, Wis. 53705.

La Tercera Reunión Ordinaria de la Cámara de Delegados se celebrará el sábado 19 de agosto en el Hotel Mayagüez Hilton, comenzando a las 9:00 a.m. Entre los asuntos a ser considerados en esta reunión se encuentra la Colegiación o no de la profesión médica, establecimiento de nuevas Escuelas de Medicina en Puerto Rico, varias enmiendas al Reglamento de la AMPR y otros.

La semana del 27 de agosto al 2 de septiembre ha sido declarada por la AMPR como "Semana de la Medicina y la Religión". El Dr. Héctor Feliciano, Presidente del Comité de Medicina y Religión, al hacer el anuncio señaló que "el propósito de esta Semana es el de crear el ambiente apropiado para la comunicación entre médicos y clérigos que conduzca a un cuidado y tratamiento más efectivo del paciente". Durante esta Semana se celebrarán una serie de conferencias sobre temas como "El Paciente Hospitalizado", "Límite de la Responsabilidad Médica en la Prolongación de la Vida" y otras de sumo interés.

El plazo para contestar el Referendum sobre construir o no un nuevo edificio de la AMPR en los terrenos de Bayamón ha sido ampliado hasta el próximo 18 de agosto. Esto se ha debido a que hasta el presente no llegan a 500 las respuestas recibidas. Se exhorta a todos los asociados que no lo hayan hecho a que envíen sus respuestas a la mayor brevedad posible.

FE DE ERRATA

Por un error involuntario, se omitió el nombre del Dr. Luis Nieves Valle, como co-autor del artículo "The Management of Acute Scrotal Swelling in Children and Young Adults" además del Dr. Roberto F. Fortuño, y publicado en el Volumen 64, Núm. 7, de julio 1972, lo que hacemos constar en esta Fe de Errata.

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Precautions: In the elderly and debili-

tated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the

elderly and debilitated. These are usually manageable in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. A few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low voltage, fast activity) may appear during treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during prolonged therapy.

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TRATAMIENTO DE LAS COMPLICACIONES DE LA CIRROSIS HEPATICA AVANZADA 219

Henry J. Tumen, MD

EL ANTIGENO AUSTRALIANO: CARACTERISTICAS Y SIGNIFICADO CLINICO 229

Ibrahim Pérez, MD

CIRUGIA RADICAL PARA TRAUMA SEVERO DEL HIGADO Y PULMON 234

Jorge O. Just Viera, MD, José I. Iglesias, MD, F. E. Oliveras Armstrong, MD, Pablo L. Morales, MD y José Raúl González Giusti, MD

HEPATITIS VIRAL: CONCEPTOS ACTUALES SOBRE ETIOLOGIA Y EL
ANTIGENO ASOCIADO A HEPATITIS (AUSTRALIANO) 238

Juan T. Tomasini, MD y Carlos Bañón, MD

HYPERBILIRUBINEMIA NOT DUE TO HEMOLYTIC DISEASE OF NEWBORN 243

Eloísa Muñoz Dones de Carrascal, MD

ACTUALIDADES MEDICAS 249

Abstractos de la Convención Anual de la
Asociación Puertorriqueña del Corazón

NOTICIAS 253

The negative power of clinically significant anxiety
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Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido — all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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*Levine, S.: "Angina Pectoris and Emotional Overlay," Scientific Exhibit presented at the Annual Meeting of the Maine Medical Association, Kennebunkport, Me., June 13-15, 1971.

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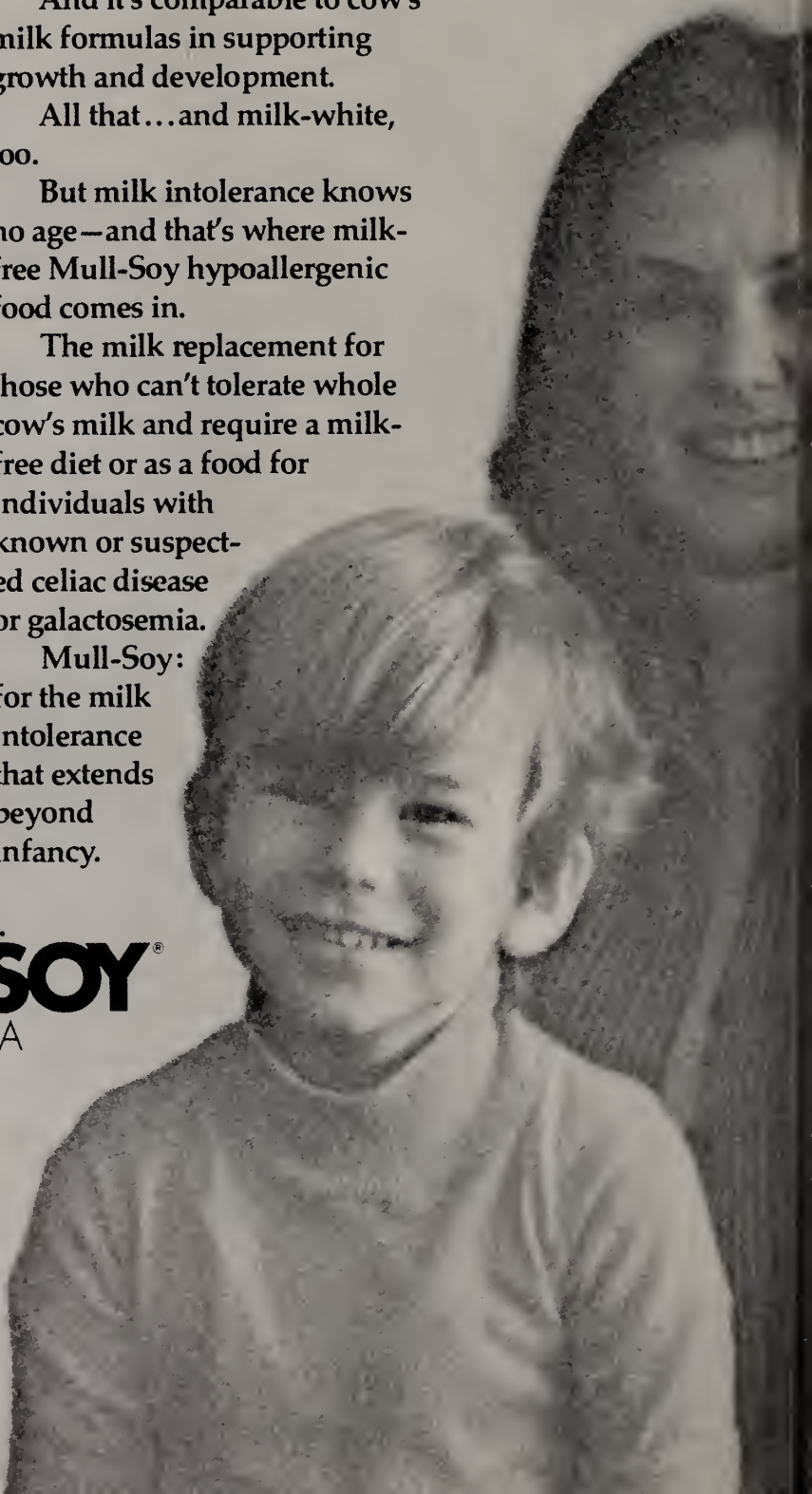
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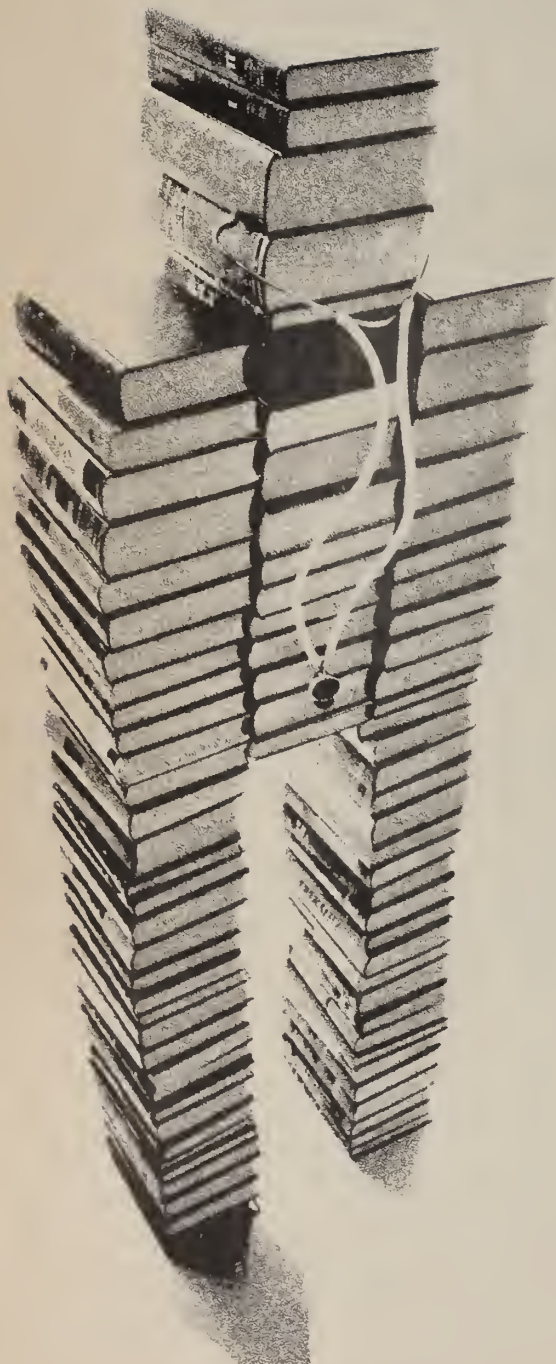
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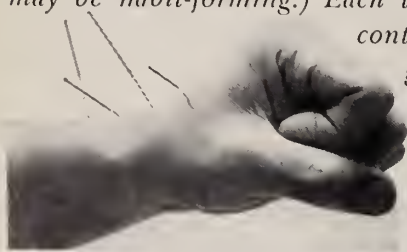
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CONFERENCIA MAGISTRAL "DR. RAMON J. SIFRE"

SEMBLANZA DEL DR. RAMON J. SIFRE

Por el Dr. A. Fernós Isern

Ante la Sociedad Puertorriqueña de Gastroenterología

Señor Presidente, Distinguidos Colegas:

Constituye un altísimo honor comparecer ante ustedes para hacer la semblanza del ilustre fundador y primer presidente de esta "Sociedad Puertorriqueña de Gastroenterología". Hablar de Ramón J. Sifre es para mí la satisfacción de revivir en el recuerdo una amistad excepcional; reencontrar en presencia, en la memoria al gran amigo desaparecido. Es ocasión de rendir homenaje a quien por tantos conceptos lo mereció en vida y lo sigue mereciendo a los diez años de haberse ausentado de nuestro mundo. Lo merecerá siempre a lo largo del tiempo.

Recordando algunos datos biográficos suyos encontramos que recibió su instrucción primaria y colegial en las escuelas y la Universidad de Puerto Rico; que inmediatamente después cursó la carrera médica en la Universidad de Pennsylvania. Hizo su internado en el Harvard Hospital de Filadelfia. Inmediatamente después ingresó voluntariamente en el cuerpo médico del ejército de Estados Unidos. Tenía lugar entonces la primera guerra mundial.

Cumplida su gestión militar fijó su residencia en Vega Alta y por espacio de once años ejerció allí su profesión. Su nombre rebasaba los ámbitos de la comarca en que residía. Se pronunciaba con respeto y admiración en los círculos médicos.

En 1930 obtuve de él que viniera a San Juan a ocupar junto a mí el cargo de Sub-Comisionado de Sanidad de Puerto Rico. Yo había sido designado Comisionado de Sanidad para aquellos días. Las circunstancias políticas eran entonces de la mayor dificultad. Era preciso mantener relaciones adecuadas entre la rama ejecutiva y la rama legislativa, en una situación política excepcional. Era de la mayor importancia que el Sub-Comisionado, alter ego del Comisionado, fuera persona de incuestionable integridad, de reconocida capacidad, de acendrada devoción al interés público. Fue el

amigo y compañero inolvidable, el Dr. Manuel Díaz García, quien me sugirió el nombre del Dr. Sifre, por quien tenía profunda admiración y a quien guardaba entrañable afecto. Le pedí encarecidamente que me acompañara a Vega Alta a solicitar de Ramón Sifre que prestara aquel servicio al país. Representaba de inmediato un sacrificio personal para él. Sin embargo logramos su aceptación.

Así se produjo su traslado de Vega Alta a San Juan. Así comenzó nuestra colaboración y se arraigó nuestra amistad que hubo de durar hasta su muerte. Perdura en el recuerdo.

No duró mucho nuestra administración del Departamento de Sanidad, hoy de Salud. Los cambios políticos ocurridos en los Estados Unidos a virtud de las elecciones de 1932, repercutieron en el gobierno colonial de Puerto Rico. A nuevo Presidente de Estados Unidos, nuevo Gobernador de Puerto Rico. Como es natural, sobrevinieron cambios en el Gabinete del Gobernador. El Comisionado y el Sub-Comisionado de Sanidad abandonamos nuestros cargos respectivos.

Devueltos ambos al ejercicio particular de la profesión no se interrumpió nuestra relación de cordial y estrecha amistad. Tuvimos nuestras oficinas contiguas. Cambiábamos impresiones casi a diario sobre asuntos profesionales, públicos, de la vida cotidiana. Pero el virus político hizo presa en mí al cabo de algunos años de latencia. Me envolví en responsabilidades y a pesar de mi desinclinación, hube de volver a ocupar el cargo de Comisionado de Salud de Puerto Rico.

Hubiera deseado contar otra vez con la colaboración del Dr. Sifre, pero no hubiera sido justo ni para él ni para con su tan extensa clientela.

Siguió él en su sacerdocio médico, devoto e infatigable. Apartado de él por mis obligaciones oficiales, que luego hubieron de llevarme incluso a la ausencia casi continua de la isla por diez y ocho años, no lo perdí de vista nunca; no se entibió nuestra amistad; no se debilitó nuestra mutua estimación. Y en cada ocasión en que retornaba yo a Puerto Rico tenía ocasión de ver que continuaba aquella labor intensa, abnegada, altruista, en su vida profesional y la misma

línea de conducta del ciudadano íntegro, ejemplar.

Perdonen los compañeros que inevitablemente estos párrafos estén tan impregnados de emoción personal. No es fácil sustraernos a esas evocaciones cuando se trata de enfocar la personalidad del Dr. Ramón J. Sifre, habida cuenta de las relaciones de amistad que tuvimos respecto de él.

Sorprendía su infatigabilidad para el trabajo; su meticulosidad para el examen y estudio de sus pacientes. Era admirable su honradez intelectual. Sus juicios eran certeros. Su criterio era recto e iluminado. Estaba al cabo de los progresos médicos en Puerto Rico y fuera de Puerto Rico.

Devoto de su familia como era, amante esposo y padre solícito, dividía su vida cuasi exclusivamente entre su hogar y sus enfermos, pero esto no le impedía mantenerse informado de los acontecimientos públicos, de las cuestiones que conmovía nuestra sociedad. Tenía gran acierto y gran penetración para interpretarlas. Era un perfecto ciudadano.

Por muchos años hizo práctica general, pero gradualmente su atención se fue enfocando en la práctica de la gastroenterología y fue un notable gastroenterólogo.

Dejó escritos trabajos médicos de gran mérito. Ante el Quinto Congreso de Gastroenterología celebrado en la Habana, presentó su trabajo sobre Sprue Tropical; ante el Sexto Congreso en Caracas presentó su trabajo sobre la ruptura no-traumática del conducto biliar común. En 1952 fue elegido fellow del Colegio Americano de Médicos.

Rindió la jornada de la vida el día 13 de septiembre de 1961. Tenía 67 años de edad. Esa es la gran tragedia del hombre, que nunca podemos comprender.

Aquella experiencia acumulada y refinada por tantos años; aquellos conocimientos cada vez más claros, cada vez más precisos, aquella fina destreza, aquel sentido claro y certero, aquel caudal inagotable de sabiduría, y aquella fuente y caudal de bien para todos, de pronto, como el cronómetro al que se agota la cuerda, cesó, dejó de ser, se perdió en la muerte inexplicable e inexorablemente.

Al cabo de una década desde su muerte comparezco ante ustedes para rendir este homenaje al amigo y compañero cuya memoria ahora evocamos. Encuentro y reconozco en esta sociedad la huella imborrable de su fundador. El penetró cuanto pudo en los secretos del cuerpo humano; en el de los procesos de sus órganos; en el de la función y la disfunción fisiológica, para despistar la enfermedad y ahuyentar la muerte. Cuando su propio cuerpo, cuando sus propios órganos se negaron a seguir dando base terrena a su mente y a su espíritu, cuando hubo él de pasar del misterio de la vida al misterio de la muerte, pudo tener (conociéndole como le conocí creo que tuvo) un último pensamiento consolador! Su obra había de continuar adelante, el progreso en el conocimiento había de seguir adelante, porque para ello quedaba esta Sociedad Puertorriqueña de Gastroenterología que él fundó, del que fue primer presidente y de la que sigue siendo inspirador. Para continuar la labor del taumaturgo que muchas veces cura y siempre consuela han quedado ustedes, distinguidos colegas, cuya es igual devoción, igual integridad profesional. Así cumplen ustedes el grato deber que la profesión impone. Con estas palabras, Señor Presidente, he tratado de cumplir el mío. Gracias a todos por haberme dado ocasión de poder hacerlo.

EL TRATAMIENTO DE LAS COMPLICACIONES DE LA CIRROSIS HEPATICA AVANZADA

Henry J. Tumen, MD

Hace veinte años, durante mi primera visita a Puerto Rico, tuve la buena suerte de conocer al Dr. Ramón J. Sifre. Inmediatamente fui atraído por su personalidad tan dulce, sus intereses culturales tan liberales, su orgullo en sus antecedentes hispánicos y lo sutil de su trato. Además, el Dr. Sifre y su señora fueron anfitriones muy amables y atentos. En un tiempo muy corto mi esposa y yo nos sentimos completamente como en nuestra casa con ellos ya que teníamos mucho en común.

En mis visitas subsiguientes a Puerto Rico conocí más y más acerca de las cualidades maravillosas del Dr. Sifre—el gran alcance de su erudición, sus altas normas éticas, su orgullo en ser médico. Además aprendí que todo el mundo compartía mi respeto y admiración por el Dr. Sifre. Verdaderamente, fue médico dilecto.

Porque me uno con ustedes en su amor por el Dr. Sifre me siento tan honrado el haber sido invitado a dar esta primera de las conferencias dedicadas a él. Estoy muy agradecido a la Asociación Médica de Puerto Rico por esta invitación. Quiero dar las gracias a ustedes por esta demostración de su amistad y por esta oportunidad de unirme a ustedes en esta demostración de cariño por el Dr. Sifre y su respeto por la memoria de un gran hombre.

La cirrosis hepática causa síntomas obvios solamente durante un breve período de su curso clínico. Los cambios estructurales del hígado progresan en forma solapada hasta que un síntoma mayor indica la presencia de la enfermedad. Desgraciadamente, la manifestación clínica inicial es frecuentemente catastrófica, dando lugar a una emergencia inmediata cuando la cirrosis ya ha alcanzado su penúltima o última etapa. Aunque comúnmente se puede controlar la emergencia, el grado del daño hepático puede ser tal que no se puede lograr una recuperación satisfactoria.

Desgraciadamente, sabemos muy poco acerca de la etiología y patogénesis de la cirrosis y de los factores que controlan su curso. Hasta es difícil definir en forma

exacta esta entidad patológica (1). Ya no es un proceso único, es la etapa avanzada, a veces la final, de muchas enfermedades hepáticas que terminan en el mismo cuadro. La lesión inicial puede haber sido causada por una sustancia tóxica como el alcohol (2); una infección, como la hepatitis viral; malnutrición; obstrucción biliar; fallo cardíaco; o una variedad de alteraciones metabólicas.

Sabemos, sin embargo, que hay muchos casos de cirrosis donde no hay evidencia de exceso de alcohol o de cualquier otra causa conocida. Para dar énfasis a esta falta de conocimiento de la etiología específica de la cirrosis, la profesora Sherlock utiliza el adjetivo "Criptogénico" (3). Se desconoce cuántos de estos casos criptogénicos comienzan como hepatitis viral. Aunque la cirrosis fuera una secuela de la hepatitis viral no sabemos si este es el resultado de la actividad continuada del virus o de una alteración en la respuesta inmunológica del paciente. Además sería un error suponer que todos los casos de cirrosis criptogénicos son idénticos y son consecuencias del mismo tipo de insulto. Es mejor admitir que pocas veces podemos hablar con certeza acerca de la etiología en un caso en particular de cirrosis. Hasta el patólogo que examina un hígado cirrótico no puede decir cómo comenzó el proceso.

Es lamentable lo poco conocido del panorama de las enfermedades progresivas del hígado porque la cirrosis es relativamente común y parece estar aumentando con frecuencia. En un año reciente murieron veintitrés mil personas por cirrosis en los Estados Unidos. En el año 1958 ocupó el octavo lugar como causa de muerte en este país (4), y fue superado solamente por enfermedades cardiovasculares, neoplasias malignas y accidentes cerebro-vasculares como causa de muerte en pacientes entre los 45 y 64 años de edad. Resulta claro que debemos estar preparados para detectarla y tratarla.

Las manifestaciones clínicas de la cirrosis varían considerablemente y no corresponden con los cambios patológicos en el hígado. Muchos de los problemas que se observan en los pacientes cirróticos no son los resultados de la cirrosis en sí sino de sus complicaciones. Estas complicaciones, tales como la hipertensión portal,

el coma hepático, y otros problemas importantes, tan comunes en la cirrosis, no son necesariamente específicos para esta enfermedad. Ocurren también en otros trastornos del hígado y del sistema portal. En forma lenta, la cirrosis de cualquier tipo alcanza sus etapas finales y ciertas manifestaciones se hacen más prominentes y asumen gran importancia. Estas son la ascitis, la ictericia, la hipertensión portal y sus complicaciones y los cambios neurológicos que pueden conducir al coma. Estas últimas dos son las causas principales de la muerte en cirrosis. Es por esta razón que al discutir el tratamiento de los pacientes cirróticos se presta tanta atención a estas manifestaciones terminales. Su manejo es siempre difícil, exigiendo gran habilidad y juicio clínico si se pretende evitar las numerosas trampas. Sin embargo, existe la recompensa, porque nuestros esfuerzos prolongan frecuentemente la vida del paciente, y por lo tanto siempre tenemos que hacer todo lo posible.

Hemorragia de Várices Esofágicas

De las emergencias que ocurren en la enfermedad avanzada del hígado las complicaciones hemorrágicas sangrantes son las más dramáticas. Este es un problema mayor que amenaza la vida del enfermo. Las várices sangrantes son el síntoma inicial en un 10 a 25 por ciento de los cirróticos. Ocurren en algún momento en 20 a 40 por ciento de los pacientes cirróticos, y son causa inmediata de muerte en un 50 por ciento (5). Un informe reciente establece una mortalidad de 67 por ciento para las várices sangrantes (6). La mortalidad elevada se debe no sólo a la pérdida de sangre sino también a la etapa avanzada de la cirrosis en el momento de la hemorragia, a la presencia de alteraciones electrolíticas, a trastornos de la coagulación, y a las deficiencias nutricionales. Otro factor que constituye una amenaza mayor es la precipitación del coma hepático por la entrada de un gran volumen de sangre en las vías digestivas. Además, como es bien conocido, los métodos disponibles para tratar las várices sangrantes son riesgosos y exponen al paciente a peligros adicionales.

La localización del punto sangrante es el primer problema que hay que afrontar cuando ocurre una hemorragia digestiva alta que se sospecha pueda ser secundaria a la cirrosis. En realidad este es un problema doble. ¿Es cirrótico el paciente, y si lo es, tiene várices esofágicas? Si las tiene, son las várices las que han causado la hemorragia?

El diagnóstico de cirrosis se basa en la historia clínica, la presencia de los signos de cirrosis (ictericia,

arañas vasculares, hepatomegalia, esplenomegalia, ascitis), y los resultados de las pruebas de funcionamiento hepático. La prueba de la bromosulfotaleína, o la determinación simple de la bilirrubina, pueden ser de inmensa utilidad en la confirmación o el rechazo del diagnóstico de cirrosis avanzada. Se puede concluir que si éstas dan resultados normales es muy poco probable que la hemorragia provenga de várices debido a cirrosis.

En el caso contrario, con retención de bromosulfotaleína y una elevación de la bilirrubina en un paciente que ha sangrado no se puede concluir que la hemorragia proviene de várices esofágicas. Una hemorragia masiva de cualquier origen puede causar algunas alteraciones del funcionamiento hepático. Aunque se demuestre que el paciente es cirrótico, aun con hipertensión portal y várices, la hemorragia puede originarse en otro sitio. Pacientes con várices pueden tener otras lesiones que pueden sangrar y frecuentemente lo hacen (7). Hasta un 50 por ciento de las hemorragias en los cirróticos provienen de lesiones que no son várices, como las úlceras pépticas, la gastritis erosiva, y los tumores gástricos. Se recomienda entonces un programa de diagnóstico agresivo para la hemorragia digestiva alta (8). El uso de la esofagoscopia, gastroscopia, exámenes radiológicos de contraste, y la angiografía abdominal (9) son de inmenso valor en la determinación del punto exacto de hemorragia en los pacientes cirróticos. Es probable que la esofagoscopia de emergencia es el examen más útil de los disponibles hasta ahora.

El tratamiento de las várices sangrantes debe incluir los esfuerzos inmediatos para controlar la hemorragia, para mantener al paciente durante este período crítico, substituir el volumen de sangre perdida, combatir el shock y evitar la temida complicación de coma hepático. Deben ser diagnosticadas y corregidas las alteraciones en la coagulación sanguínea. La sangre utilizada debe ser lo más fresca posible para proporcionar los factores de coagulación y sus plaquetas que la sangre de banco pierde. En algunos pacientes son de utilidad los agentes que contrarrestan las fibrinolisin. Debe corregirse cualquier desequilibrio electrolítico, especialmente la hipocalcemia.

Para evitar el coma hepático debe eliminarse la sangre acumulada en las vías digestivas, por medio de la aspiración gástrica, de enemas y laxantes salinos, y a la vez evitar la descomposición bacteriana de las proteínas sanguíneas con la administración de neomicina o de otro antibiótico apropiado.

Entre las medidas para controlar la hemorragia de várices esofágicas, el taponamiento con la sonda de Sengstaken Blakemore ha sido usado en forma extensa.

Con buen uso y con supervisión cuidadosa, esta sonda controla la hemorragia por lo menos en forma temporera en la mayoría de los pacientes. En algunos pacientes el taponamiento parará la hemorragia permitiendo el retiro de la sonda después de pasada la emergencia. Esto no es lo usual, y además, el tratamiento por taponamiento tiene riesgos, y requiere gran habilidad, buen juicio, y excelente cuidado de enfermería. Entre las muchas complicaciones del taponamiento debe subrayarse la obstrucción de las vías respiratorias, la regurgitación, la aspiración bronquial con pulmonía, y la ruptura del esófago por desgarre. Conn ha informado que sólo un 20 por ciento de los pacientes tratados por taponamiento no tuvieron complicaciones potencialmente fatales (10). No es un método a utilizarse sin una supervisión adecuada.

La vasopresina (Pitresina) es útil para controlar la hemorragia por várices esofágicas (11). Al reducir la circulación mesentérica esta droga reduce la presión portal. Generalmente se administran veinte unidades en veinte a treinta centímetros cúbicos de solución glucosada por vía endovenosa durante un período de diez a quince minutos. Su efecto es transitorio y frecuentemente hay que repetir la dosis a intervalos de una a dos horas. Aun así, puede no lograrse una hemostasis prolongada y deben tenerse en cuenta los muchos efectos secundarios producidos por la droga: dolores cólicos, diarrea, y en pacientes con patología coronaria, su acción vasoconstrictora puede causar un infarto. En el Graduate Hospital hemos desarrollado un método de administración de pitresina en cantidades muy pequeñas directamente en la arteria mesentérica superior bajo control arteriográfico, permitiendo el control eficaz de la hemorragia.

Cuando, a pesar de las medidas descritas, continúa la hemorragia y si la condición del paciente es demasiado grave para tolerar una anastomosis porto-cava, puede intentarse alguna medida quirúrgica más conservadora. Orloff ha recomendado la ligadura transesofágica de las várices (13) como un tratamiento muy eficaz en una emergencia. Sin embargo, debe ser seguido por una anastomosis porto-cava tan pronto el paciente recupere, porque la ligadura de las várices es, cuando mucho, una medida para ganar tiempo. Cabe preguntar si el riesgo combinado de la ligadura transesofágica seguida por la anastomosis porto-cava no es mayor que el riesgo de proceder con la anastomosis inicialmente.

Si se detiene la hemorragia, aún queda la necesidad de considerar la anastomosis porto-cava que bajará la presión en el sistema portal, reduciendo la posibilidad de otra hemorragia. Esta decisión exige un alto grado

de juicio clínico por parte del internista, y gran habilidad por parte del cirujano. Estos pacientes tienen una seria alteración hepática con pérdida de sangre, shock, precoma hepático y defectos hematológicos. Ofrecen un riesgo quirúrgico grave. Sin embargo, de repetirse la hemorragia, el riesgo se multiplica por el deterioro hemodinámico que resulta. Existe, pues, una sensación de urgencia para evitar la hemorragia adicional.

Todos los estudios sobre los resultados de las anastomosis porto-cava han indicado la relación estrecha del riesgo operatorio con el estado funcional del hígado y el estado general del paciente al tiempo de la intervención. En los pacientes óptimos, la mortalidad operatoria es baja, pero aumenta bruscamente con ictericia, una sero-albúmina baja o con encefalopatía. Desgraciadamente, el tratamiento médico puede no producir una mejoría en el estado del hígado, y puede ser interrumpido por otra hemorragia. Por esto hay muchos que recomiendan una anastomosis porto-cava tan pronto se detiene la hemorragia, salvo que exista evidencia de un deterioro rápido de la función hepática o indicaciones de coma hepático. En muchos casos el riesgo de otra hemorragia parece mayor que el de la cirugía.

La selección del momento apropiado para la operación es de suma importancia. La mejoría de la función hepática y el nivel de las proteínas séricas, ocurre raramente. Frecuentemente es necesario someter al paciente tal como está, y proceder con una operación mayor en condiciones que dejan de ser ideales. El médico frecuentemente tiene que hacer lo mejor que puede en situaciones difíciles.

Como estos desvíos quirúrgicos reducen tan impresionantemente la frecuencia de las hemorragias esofágicas se ha aconsejado su uso profiláctico. Este punto, sin embargo, no ha recibido apoyo en investigaciones controladas. El grupo de investigaciones hepáticas interhospitalarias de Boston (14), y Conn y Lindemuth (15), han demostrado que, en los pacientes estudiados, las anastomosis porto-cava profilácticas no aumentan la longevidad de cirróticos con várices. Es raro que pacientes con anastomosis mueran como consecuencia de hemorragias, pero la intervención no evita el deterioro hepático progresivo ni el fallo renal consecutivo a menos que mejore el estado funcional hepático.

A pesar de esta observación pesimista debe señalarse que en algunas series la longevidad es larga después de una anastomosis. McDermott y colaboradores informaron que un 70 por ciento de sus pacientes vivieron más de cinco años después de la cirugía. Resultados tan buenos como estos se han logrado

al evitar que progrese el deterioro hepático, mejorando el estado de nutrición, y protegiendo el hígado de los efectos de agentes tóxicos, de los cuales el más común, por supuesto, es el alcohol.

Los pacientes operados se ven amenazados por otros problemas que se enumeran en la lista siguiente: 1) Encefalopatía; 2) Úlcera péptica; 3) Hemoeromatosis; 4) Hipoglucemia y diabetes; 5) Alteraciones en el funcionamiento hepático; 6) Hiperesplenismo; 7) Hepatoma.

De éstas, debe subrayarse la importancia de la encefalopatía, notada en un 25 a 35 por ciento de todos los pacientes que sufren una anastomosis porto-cava. Su frecuencia aumenta en los pacientes que son operados después de los 40 años de edad. Es también cierto que cuánto más tiempo viva el paciente después de la anastomosis, mayor es la frecuencia de la encefalopatía.

La encefalopatía siempre constituye una amenaza, y debe tratarse rápidamente si ésta se manifiesta.

Coma Hepático

El paciente con insuficiencia hepática avanzada se ve también amenazado por el desarrollo de síntomas neurológicos y mentales, desde cambios mínimos en la personalidad, confusión, desorientación, estupor, hasta el coma, manifestaciones conocidas como "encefalopatía hepática". Se usa más "coma hepático", a pesar de que puede no ocurrir un coma verdadero. La encefalopatía puede ser consecuencia de cualquier proceso que reduzca la capacidad funcional metabólica del hígado, ya sea destruyendo hepatocitos, o por la formación de cortocircuitos que permiten el tránsito de grandes cantidades de sangre portal a la circulación general sin haber atravesado el hígado. La causa más común es la cirrosis que combina la destrucción de hepatocitos con el cortocircuito porto-sistémico ya sea espontáneo o construido quirúrgicamente. El coma es el mecanismo de muerte en aproximadamente un tercio de los casos fatales de cirrosis (17).

En pocas palabras, el coma hepático puede considerarse como una especie de intoxicación cerebral causada por sustancias intestinales que no han sido metabolizadas por el hígado. Otra posibilidad es que el coma sea consecuencia de alteraciones metabólicas relacionadas con el mal funcionamiento hepático que hacen que el cerebro sea más susceptible a una variedad de toxinas y alteraciones fisiológicas (18). Los mecanismos bioquímicos que conducen al coma no han sido clarificados en forma adecuada, y es posible que el mecanismo sea distinto bajo diferentes circunstancias. La opinión más aceptada es que el coma lo causa una substancia

de origen protéico, el amoníaco, formado en el intestino como resultado del metabolismo bacteriano. Este amoníaco metabolizado en forma incompleta ya sea por la enfermedad que afecta a los hepatocitos o por la desviación de la sangre portal, alcanza el cerebro e interrumpe los ciclos metabólicos que proveen al sistema nervioso la energía esencial para su funcionamiento. Este concepto del coma probablemente es correcto en muchos casos, pero no explica todos los ejemplos de coma hepático. También pueden ser responsables las alteraciones metabólicas de los hidratos de carbón, aminoácidos, ácidos grasos de cadena corta, electrolitos o compuestos azufrados (19). En muchos casos la encefalopatía es provocada por factores adicionales que agregan una carga metabólica excesiva sobre un hígado ya gravemente enfermo. Este tipo de coma ha sido llamado "exógeno" (20).

Los factores que precipitan el coma y los mecanismos de sus influencias dañinas se detallan en la siguiente lista:

CAUSAS PRECIPITANTES DEL COMA HEPATICO

Causa	Mecanismo
1. Proteínas en exceso	Producción aumentada de amoníaco en el intestino.
2. Hemorragia digestiva	Producción aumentada de amoníaco de las proteínas sanguíneas. Producción aumentada de amoníaco de la urea que resulta del mal funcionamiento renal. Amoníaco en la sangre transfundida, que aumenta cuanto más vieja es la sangre. El shock y la hipoxia.
3. Diuréticos	Disminución de potasio, causa la liberación de mayor cantidad de amoníaco de los riñones. Alcalosis, aumenta el tránsito de amoníaco al parénquima cerebral.
4. Paracentesis	Pérdida de potasio. Reducción del contenido intravascular y deterioro en el funcionamiento renal.
5. Infecciones y Cirugía	Daño a los tejidos. Demandas metabólicas aumentadas.

- | | |
|---|--|
| | Deshidratación y deterioro en el funcionamiento renal. |
| 6. Uremia | Formación aumentada de amoníaco de la urea. |
| 7. Sedantes, anestésicos y, en especial, la morfina | Efecto deprimente directo sobre el cerebro. |

Es evidente que hay muchos factores que contribuyen a la producción del coma, y que el proceso crítico es la interferencia con la liberación de la energía necesaria para el funcionamiento cerebral. Por esta razón merecen mucha atención las alteraciones y los efectos de los transmisores neuro-químicos. Sustancias como la levodopa quizás sean de utilidad en el tratamiento, aunque los estudios correspondientes aún se encuentran en su etapa preliminar (21).

Debe enfatizarse el peligro de administrar morfina, aún en dosis pequeñas, a pacientes con encefalopatía incipiente u otros síntomas indicativos de enfermedad avanzada del hígado. Aún con estas dosis se han demostrado cambios electroencefalográficos y clínicos de encefalopatía, y por eso deben evitarse.

Es muy importante reconocer las etapas iniciales de la encefalopatía, la "Pre-Coma", para iniciar el tratamiento con suficiente tiempo y evitar el desarrollo del coma verdadero, que con su rápido deterioro frecuentemente conduce a la muerte. Cuando la insuficiencia hepática ocurre en el transcurso de una hepatitis fulminante el coma y la muerte pueden ocurrir muy rápidamente, con manifestaciones premonitorias mínimas. En los cirróticos las manifestaciones neurológicas y mentales progresan mucho más lentamente. Las indicaciones iniciales pueden estar presentes durante días o semanas o aún más, antes de que el paciente se vuelva estuporoso y, finalmente, comatoso. El clínico alerta debe estar atento a estas señales de peligro, que incluyen cambios mínimos en la personalidad o en el comportamiento, falta de proligidad en las acciones, cambios en el lenguaje hablado y pérdida de la agudeza mental.

Acompañan estas alteraciones la incoordinación muscular manifestada al intentar la construcción de diseños sencillos, y por el deterioro al escribir. El paciente muestra generalmente un signo característico del pre-coma, el "flap". A medida que el cuadro progresa se agrega la confusión, la agitación y hasta el delirio. Si en este momento el paciente recibe un sedante en lugar del tratamiento necesario es muy probable que entrará en coma verdadero con consecuencias fatales.

Uno de los grandes peligros, pues, es el no reconocer el proceso. Si se identifican las etapas iniciales de la

encefalopatía y se procede con el tratamiento adecuado puede producirse una mejoría rápida en el cuadro clínico. Si existe alguna duda acerca de la causa de los síntomas el diagnóstico puede ser apoyado buscando los cambios electroencefalográficos característicos, las ondas lentas y de gran amplitud. Este es un método más exacto para el reconocimiento del pre-coma que la determinación del nivel del amoníaco sanguíneo, pero aún en la presencia de un electroencefalograma lamínima sospecha de la existencia de pre-coma debe llevar a la iniciación de un programa de tratamiento.

Los pasos en el tratamiento del coma hepático han sido indicados en la discusión de los mecanismos que lo causan. Las medidas iniciales más importantes consisten en abolir la proteína ingerida e inhibir la degradación bacteriana de las sustancias protéicas en el intestino. La alimentación se reduce a jugos de frutas azucarados y otros hidratos de carbono. Si estos no son bien tolerados puede administrarse una solución glucosada intravenosa. Debe vaciarse el intestino con enemas y laxantes salinos. Esto es de especial importancia cuando se pretende evitar el coma que sigue a una hemorragia digestiva. Las proteínas en la dieta se reintroducen gradualmente cuando el paciente mejora, comenzando con veinte gramos diarios y escalando en aumentos de veinte gramos cuando se demuestra que el paciente tolera bien la cantidad permitida. Deben recetarse vitaminas y corregir el desequilibrio electrolítico, especialmente la hipocalcemia. Es necesario evitar los narcóticos y los barbitúricos. Si se debe utilizar un sedante, quizás el mejor sea el Benadryl.

Para reducir la acción bacteriana en el intestino la neomicina tiene los mejores resultados. Sus efectos tóxicos son poco frecuentes, con dosis inicial de seis a ocho gramos y luego, cuatro gramos. Las proteínas en la dieta pueden aumentarse gradualmente mientras el paciente sigue con neomicina. Cuando se tolera sesenta a setenta gramos de proteína diaria se reduce la dosis de neomicina y se discontinúa si no hay indicación de encefalopatía. Frecuentemente es necesario continuar con cuatro gramos de neomicina diariamente durante un período indefinido para permitir así que el paciente coma una cantidad satisfactoria de proteínas. El uso reciente de Lactulosa, un disacárido que no es absorbido y que reduce la absorción de amoníaco del intestino parece permitir ingerir mayor cantidad de proteínas sin el uso de neomicina. Se ha demostrado que reduce las recurrencias de la encefalopatía y es un método nuevo en el tratamiento de la encefalopatía que merece ser explorado más (22).

Estas medidas generalmente bastan si son instituidas

en los comienzos del pre-coma y si el daño hepático no es demasiado avanzado. Aún en casos con coma verdadero, la eliminación total de proteínas, la administración de neomicina y de soluciones dextrosadas y la evacuación intestinal frecuentemente bastan para reestablecer el conocimiento y para conducir a una mejoría.

Otras medidas que han sido utilizadas no han demostrado ser de mucho beneficio. La arginina y el ácido glutámico, aceptados en el pasado con entusiasmo, no han demostrado ser de beneficio alguno. Los corticoesteroides tampoco han ayudado en el tratamiento del coma en los cirróticos. Solamente en raras ocasiones ha sido tratado exitosamente el coma cirrótico con medidas heroicas tales como la exsanguíneo-transfusión, la perfusión de hígados heterólogos y la hemodiálisis. Se debe enfatizar que lo más necesario en el tratamiento del coma es mantener vivo al paciente durante un período de tiempo. El hecho de que puede ocurrir cierta recuperación hepática justifica todo esfuerzo que se haga para continuar con el tratamiento disponible, aún en presencia de un coma que se profundiza.

En el paciente que recuperado del coma, es amenazado por posibles recurrencias, se requiere ciertas medidas preventivas, como disminución de proteínas en la dieta, neomicina en dosis pequeña, posiblemente la Lactulosa, administración de potasio, uso juicioso de diuréticos que causan pérdida de potasio, tratamiento inmediato del estreñimiento y observación constante para detectar los primeros indicios de la encefalopatía, y emplear medidas más vigorosas. Para aquellos pacientes que continúan sufriendo de episodios de coma a pesar de todo tratamiento se ha recomendado la operación de exclusión colónica. Estas operaciones a veces han parecido ser beneficiosas, pero se necesitan muchos estudios bien controlados antes de que su valor quede firmemente establecido (23).

La Insuficiencia Renal

La última de las complicaciones importantes de las enfermedades avanzadas del hígado que quiero discutir es la insuficiencia renal. No entraré en los detalles de la retención de sodio y líquidos que ocurre tan comúnmente en los cirróticos, ni hablaré de la ascitis que es frecuentemente el síntoma más llamativo. Los cambios fisiológicos y bioquímicos que conducen a la retención de líquidos en la cirrosis son ahora bastante bien entendidos. Son características típicas de la cirrosis la presión oncótica reducida como consecuencia de la hipoalbuminemia, la retención de sal y de agua, el hiperaldosteronismo

y los cambios hormonales relacionados. Los mecanismos que inician la retención de sodio son más oscuros y no conocemos bien como se inicia la ascitis. Lo que sabemos nos basta para tratar estos problemas de retención de líquidos cuando ocurren en los cirróticos. El empleo de una dieta baja en sodio y la restricción de líquidos, como también el uso de los diuréticos modernos y los antagonistas de la aldosterona son parte del manejo diario de esta enfermedad.

Si los cirróticos son protegidos de los efectos letales de las otras complicaciones y viven durante períodos largos, el mal funcionamiento renal se convierte en un problema de mayor importancia. Es así que en un grupo de cirróticos con várices que fue seguido hasta la

muerte el 12 por ciento falleció de insuficiencia renal. Esta complicación promete ser el factor más importante en la determinación del pronóstico final de la cirrosis.

Los estudios iniciales fueron dirigidos a la búsqueda de cambios estructurales en los riñones para explicar las alteraciones renales de los cirróticos. Se descubrieron varias anomalías glomerulares y tubulares pero ninguna de ellas fue encontrada en forma consistente, ni se consideraron específicas para la cirrosis. Los estudios más recientes parecen dejar bien establecido que la insuficiencia renal en la cirrosis se debe más a una alteración funcional que orgánica. Koppel *et al* (24) han demostrado que los riñones de pacientes que habían fallecido debido al síndrome hepato-renal funcionaban muy bien cuando eran transplantados a recipientes con nefropatías terminales pero con hígados normales.

La causa del fallo renal en la cirrosis avanzada es aún tema de investigación. Los estudios de años recientes parecen indicar como el factor principal la presencia de cambios hemodinámicos en el riñón mismo. Ocurre una reducción en la perfusión renal, un aumento en la resistencia, en la filtración glomerular y una redistribución de la circulación sanguínea de tal forma que disminuye el volumen de sangre que va a la corteza renal. Desgraciadamente, la naturaleza y la causa de estos cambios no son conocidos. Debido a que la uremia suele presentarse en forma abrupta en estos casos, es posible que sea resultado de una mínima pero crítica reducción en el volumen extracelular efectivo, ya de por sí reducido, a una redistribución inaparente de los líquidos corporales, o a un cambio en la respuesta del riñón a la prolongada reducción del volumen extracelular. La causa más obvia de la reducción del volumen efectivo en los cirróticos es el estancamiento de sangre en los vasos mesentéricos como consecuencia de la hipertensión portal. Hay además otras anomalías de la distribución de sangre en los cirróticos que pueden tener

importancia en la producción de cambios en la circulación renal. Estos incluyen los cortocircuitos entre las venas porta y pulmonar, entre capilares y arteriolas y los cambios en la piel, tales como arañas vasculares y el eritema que son indicios de vasodilatación. Los efectos de cada uno de estos puede ser pequeño pero cuando se suman resultan en un aumento del espacio vascular y una reducción del contenido efectivo. Cuando el volumen sanguíneo es aún más reducido y particularmente cuando esto ocurre bruscamente por una hemorragia masiva, la alteración hemodinámica asume un papel de mayor importancia y puede producirse insuficiencia renal.

Los aspectos clínicos y bioquímicos del fallo renal en los cirróticos incluyen oliguria pronunciada, hipotensión, uremia, hiponatremia marcada e hipocalcemia. La insuficiencia renal puede ocurrir en forma repentina y causar la muerte en poco tiempo. A veces es consecuencia de una paracentesis o de una hemorragia y puede ocurrir también durante el coma hepático. No existe una relación constante con el grado de ictericia o con el volumen de la ascitis. Sin embargo, el mejoramiento de la función renal que acompaña a un mejoramiento en el estado del hígado dá apoyo a la opinión de que el proceso renal es secundario a la enfermedad hepática. A veces el comienzo del fallo renal indica un cambio de dirección en el curso de la enfermedad, con evolución fatal. El grado de la hiponatremia es un guía pronóstico de valor, y es muy raro que ocurra en recuperación cuando el sodio cae por debajo de 130. La uremia marcada con niveles por encima de 100 mgs. por 100 cc de sangre también indica un final cercano. Se asigna el término "síndrome hepato-renal" a esta forma de insuficiencia renal, aunque esta frase fue usada anteriormente para designar el fallo renal que ocurría después de una operación para obstrucción biliar crónica.

El tratamiento actual del síndrome hepato-renal no es muy satisfactorio. Debe mantenerse el volumen sanguíneo efectivo con transfusiones de sangre, plasma y albúmina baja en sodio. Al aumentar el volumen intravascular puede ocurrir diuresis. Las soluciones glucosadas concentradas son beneficiosas. Debido a la diuresis reducida existe el peligro de sobrecargar la circulación. Trabajos recientes han sugerido que el metaraminol (aramina) puede ser bastante útil en el tratamiento del fallo renal en los cirróticos, especialmente si se aumenta el volumen sanguíneo (25). Su mecanismo de acción se desconoce pero puede estar vinculado a cambios en la distribución de sangre dentro del riñón.

Vuelvo a enfatizar que las complicaciones de la cirrosis que he señalado — la hemorragia de várices esofágicas, el coma y la insuficiencia renal son complicaciones de

una enfermedad muy avanzada. Se deben realizar esfuerzos para evitarlas en lo posible, ya que el tratamiento es tan poco efectivo. El control de cualquiera de estas complicaciones no significa que el proceso cirrótico ha sido vencido, sino solamente que un síntoma serio ha sido controlado. El paciente todavía tiene su enfermedad hepática. Su destino final dependerá no solo en evitar la recurrencia de complicaciones, sino más básicamente en la habilidad de restaurar la función de su hígado.

Por lo tanto, el médico no puede estar contento tratando solamente una complicación de la cirrosis. Tiene que tratar al paciente en su totalidad para darle la mejor posibilidad de sobrevivir.

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EL ANTIGENO AUSTRALIANO: CARACTERISTICAS Y SIGNIFICADO CLINICO

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Aunque la hepatitis viral ha sido reconocida por siglos, no fue hasta la Segunda Guerra Mundial que se consideró definitivamente como una enfermedad primaria del hígado. Quedaron establecidos, entre otros, los siguientes conceptos: existencia de por lo menos dos tipos, infecciosa y sérica, con transmisión oral-fecal y parenteral respectivamente; diferentes períodos de incubación; y la etiología viral de la enfermedad sugerida a base de los experimentos de transmisión usando suero y contenidos intestinales.

Estudios subsiguientes en la Escuela Estatal de Willowbrook en Nueva York bajo la dirección de Krugman (1) confirmaron claramente la presencia de dos tipos de hepatitis epidemiológica e inmunológicamente diferentes. La primera, hepatitis infecciosa (III, MS1) es transmitida por vía oral y parenteral con período de incubación corto (30-38 días) mientras que la hepatitis "sérica" (SH, MS2), con igual transmisión oral y parenteral tiene un período de incubación largo (41-108 días). La similitud en la forma de transmisión fue una de las grandes revelaciones de los estudios de Krugman restándole fuerza al término hepatitis "sérica" y a los conceptos prevalecientes de su transmisión parenteral exclusivamente. Además, la forma de transmisión no afecta el período de incubación de la hepatitis MS1, pero es más prolongado después de la transmisión oral comparado con la parenteral en la hepatitis MS2. Aunque el cuadro clínico, perfil químico, anatomía patológica, y muchos de los aspectos epidemiológicos de la enfermedad han quedado relativamente bien definidos, sin embargo, numerosos intentos para cultivar, propagar, e identificar el virus o virus causantes de la hepatitis no han tenido éxito.

La búsqueda moderna del agente o agentes causantes de la hepatitis comenzó en 1961 durante el curso de un estudio para determinar las variaciones hereditarias en las proteínas séricas. Blumberg (2) y su grupo

detectaron la presencia de un anticuerpo en el suero de un paciente con hemofilia que había recibido múltiples transfusiones. Este anticuerpo reaccionaba con el antígeno presente en el suero de un aborigen australiano pero no con una variedad de otros sueros estudiados. Este nuevo antígeno descubierto fue denominado Antígeno Australiano. Inicialmente, este antígeno fue detectado en una pequeña porción de la población normal de los Estados Unidos, pero con una frecuencia más significativa en personas normales de países Asiáticos y Oceánicos y en pacientes con el síndrome de Down, leucemias y lepra lepromatosa (3, 4, 5). En 1966 la asociación con hepatitis fue claramente establecida y desde entonces han surgido nuevos nombres para el antígeno: antígeno de la hepatitis, antígeno SH, y antígeno asociado con hepatitis (AAH).

Características del Antígeno de la Hepatitis (AAH)

1. Especificidad

Cuando se analizaron los sueros de los pacientes estudiados por Krugman en Willowbrook, se detectó la presencia del AAH en 97 por ciento de las hepatitis MS2, y su ausencia en 41 casos consecutivos de hepatitis MS1 (6). Sin embargo, en otros informes, se sugiere la presencia del AAH en la hepatitis infecciosa (7). Esta discrepancia en la asociación del AAH con hepatitis puede atribuirse a la dificultad en diferenciar hepatitis infecciosa MS1 de hepatitis "sérica" MS2 a base de la información clínica solamente. Los pacientes con hepatitis sin historial de inyección parenteral generalmente se diagnostican como del tipo MS1. Por el contrario, el término hepatitis "sérica" se reserva para situaciones donde hay historial de inoculación parenteral. Establecido ya que ambos tipos pueden ser transmitidos por vía oral y parenteral, la información de contacto puede conducir a conclusiones erróneas. Los casos de Krugman, sin embargo, representan series puras de los tipos individuales de hepatitis que permiten conclusiones más definitivas de la relación AAH-hepatitis.

2. Presencia en Sangre

Del Departamento de Medicina, Escuela de Medicina de la Universidad de Puerto Rico. Presentado ante la 4ta. Conferencia en Medicina Diagnóstica del Caribe. San Juan, P. R., marzo 6-8, 1972.

El AAH puede detectarse en la sangre de los pacientes con hepatitis MS2 temprano en el período de incubación, esto es, de 2 semanas a 2 meses, antes del comienzo de las manifestaciones clínicas o bioquímicas de la enfermedad hepática. El antígeno en el suero es detectable de forma transitoria y generalmente desaparece a las 5-6 semanas de haber comenzado el cuadro clínico.

3. Localización

Por pruebas de fluorescencia se ha demostrado la presencia del AAH en los núcleos de las células hepáticas en pacientes con hepatitis y AAH positivo en su sangre (8). Se ha detectado el antígeno en la orina, saliva, heces fecales, líquido sinovial y líquido ascítico, además de la sangre.

4. Pruebas de detección

La detección del AAH se hizo en los estudios iniciales usando la difusión en agar gel, que luego probó ser un método poco sensitivo. Actualmente, la inmunoelectroforesis es la técnica más fácil de usar como investigación rutinaria, no especializada, con resultados rápidos y sensibilidad muy aceptable. Otras técnicas más especializadas y sensitivas incluyen la de fijación de complemento, la de ensayo radioinmune y la de hemaglutinación (9).

5. Caracterización

Luego de establecida una relación del antígeno con la hepatitis MS2, cabe preguntar. ¿Qué es verdaderamente el AAH? ¿Es el virus de la hepatitis?

El antígeno fue aislado del suero humano por ultracentrifugación para estudio. Al inspeccionar las fracciones de suero conteniendo el antígeno con el microscopio electrónico se encuentran partículas de alrededor de 42 nm., en forma de palillos de tambor, y partículas más pequeñas (20 nm.), esféricas y largas. Dane y otros investigadores (10) sugieren que las partículas más grandes representan el virus de la hepatitis mientras que las pequeñas son el antígeno, producto de degradación del virus, o quizás, el material protéico capsular que contiene los determinantes antigénicos del virus. Grady cree que el antígeno es el virus y que no hay razón de peso para rechazar esta interpretación sencilla. El antígeno parece ser el virus o parte de él. A pesar de estos adelantos no ha sido posible cultivar o aislar definitivamente el virus causante de la hepatitis.

Implicaciones Clínicas

Ya establecido el rol del AAH como posible agente de la hepatitis MS2, sus implicaciones clínicas pueden

enumerarse, como aquellas de valor diagnóstico, valor pronóstico, valor epidemiológico, valor preventivo y valor etiológico.

1. Valor Diagnóstico

La especificidad del AAH para identificar la hepatitis "sérica" provee una excelente prueba diferencial de los dos tipos de hepatitis viral (11). El AAH es el único marcador definitivo para el diagnóstico de la hepatitis MS2 debido a la insuficiencia de la información clínica para establecer una distinción clara entre los dos tipos de hepatitis. Una prueba positiva de AAH en el suero es indicativa de infección con el virus MS2, presente o pasada. Una prueba negativa, sin embargo, no descarta el diagnóstico ya que el antígeno ocurre en forma transitoria y puede no ser detectable en un momento dado, o que la técnica de detección no sea suficientemente sensitiva para captar títulos bajos del antígeno en el suero. Una prueba negativa puede, además, ser indicativa de que el paciente padece de la hepatitis tipo MS1.

Desde el punto de vista diagnóstico, es importante reconocer el valor de distinguir cuál de los dos tipos de hepatitis está presente. La evidencia disponible demuestra que la hepatitis infecciosa MS1 es una enfermedad benigna que en muy raras ocasiones produce enfermedad hepática fulminante, crónica o progresión a cirrosis. Por el contrario, aunque la hepatitis MS2 es benigna en la mayoría de los casos, la mortalidad, severidad y frecuencia de progreso a cirrosis es más seria. Por esta razón, el AAH como prueba de diagnóstico marca el tipo de hepatitis que tiene mayor propensión a ocasionar dificultades al paciente, precisamente el tipo de más interés clínico.

2. Valor Pronóstico

En la mayoría de los pacientes con hepatitis MS2 el antígeno desaparece de la sangre en 4-6 semanas después de comenzar los síntomas. La persistencia del antígeno en la sangre por un período de más de 13 semanas ocurre en menos de 5 por ciento de los casos, pero en este grupo la mayoría desarrolla hepatitis crónica, como fue demostrado en la serie de Nielsen en Copenhagen (12). Redeker (13) encontró que en todos los casos de hepatitis que habían progresado a cirrosis habían sido aguda y crónicamente positivos para AAH y que la enfermedad crónica no se desarrollaba en pacientes negativos para el AAH. El progreso a cirrosis era evidente en un período de 12-18 meses. Luego de una hepatitis AAH positiva hay un grupo pequeño con antígeno persistente sin evidencia de enfermedad hepática que entran a asumir el rol de

portadores de la enfermedad en su sangre.

3. Valor Epidemiológico

Desde el advenimiento de la prueba del AAH se ha podido confirmar la transmisión oral-fecal de la hepatitis MS2. Esto invalida la terminología de "se-rica" para este tipo de hepatitis para eliminar la implicación de que sólo se transmite por vía parenteral como se creía originalmente. El antígeno ha sido detectado con mayor frecuencia en pacientes con el síndrome de Down en instituciones grandes relacionado en parte a las pobres condiciones sanitarias prevalecientes. Además se encuentra con más frecuencia en enfermedades crónicas donde el mecanismo de inmunidad está alterado como las leucemias, linfomas, lepra y enfermedad renal crónica tratado con hemodiálisis. Muchos de estos pacientes padecen de hepatitis crónica, frecuentemente anictérica y representan un depósito enorme de infección que puede ser un riesgo para el personal que los atiende. Brotes de hepatitis han sido informados en unidades de diálisis incluyendo a pacientes y personal médico.

El descubrimiento del Antígeno Australiano ha abierto una brecha interminable con relación a la posible contaminación por diversos mecanismos como picadas de insectos, relaciones sexuales, besos, contaminación de equipo de barbería, quirúrgico y dental y especialmente personal de laboratorio y bancos de sangre. La prueba del AAH puede ser utilizada para detectar brotes que puedan afectar estos grupos a riesgo.

Cuando se estudian los brotes epidémicos y esporádicos de hepatitis con la prueba del AAH se encuentra que los brotes de hepatitis MS1 son particularmente frecuentes en niños y adolescentes y en situaciones donde se puede trazar el brote a un foco de contaminación como en el caso de la epidemia en la Universidad de Holy Cross (14). En la hepatitis esporádica con o sin historial de contacto con agujas contaminadas o en casos post-transfusión sobre 50 por ciento son AAH sin historial de contacto con agujas contaminadas o en casos post-transfusión sobre 50 por ciento son AAH positivos (15). Esto indica que la hepatitis MS2 probablemente sea la mayor causa de hepatitis esporádica en adultos de zonas urbanas irrespectivo de la presencia o no de un historial de infusión de sangre contaminada o sus productos. Es posible que los adultos sean relativamente inmunes a la hepatitis infecciosa MS1 y por lo tanto, la infección con MS2 sea más frecuente.

4. Valor Preventivo

a) donantes de sangre

Algunos donantes de sangre poseen una prueba AAH positiva. En la población general de donantes esta

cifra es alrededor de 0.1 - 0.5 por ciento pero es considerablemente mayor en donantes comerciales, prisioneros, adictos y residentes de áreas urbanas pobres y congestionadas. Estos grupos constituyen una fuente importante en la transmisión del virus de la hepatitis. Cuando un paciente recibe sangre AAH positiva varias situaciones pueden ocurrir (16). Puede que no se produzca enfermedad hepática y que el antígeno no sea detectable en su sangre o que se detecte y persista como portador. Puede desarrollarse una hepatitis aguda, de severidad variada, desde subclínica a fulminante, con el antígeno eventualmente desapareciendo de la sangre y con el hígado retornando a normal o desarrollando cirrosis. En algunos casos el AAH persiste y el paciente se convierte en un portador asintomático o con evidencia de enfermedad hepática crónica. Biopsias hepáticas en estos pacientes pueden mostrar un hígado normal o cirrótico, o hepatitis crónica persistente o agresiva con o sin cirrosis. Estas diferentes situaciones se esquematizan en la figura número uno.

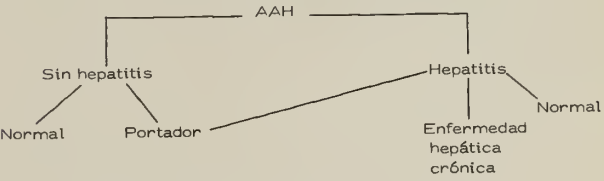


Fig. 1: Efectos del AAH en el Recipiente.

Los factores más importantes que determinan el curso clínico del paciente son: la dosis de virus recibida, su virulencia y la respuesta inmunológica del paciente.

Estudios de la frecuencia de hepatitis en pacientes que reciben sangre AAH positiva revelan un riesgo para el recipiente de 40-70 por ciento (17, 18). Por esta razón, la prueba de AAH en donantes se ha convertido en un procedimiento de rutina en los bancos de sangre. La prueba es mandatoria en los bancos de sangre de la Cruz Roja Americana y desde fines de 1971 en los bancos de sangre de la Asociación Americana de Bancos de Sangre (19).

Aunque se espera una baja significativa en la frecuencia de hepatitis post-transfusional al eliminar todos los donantes positivos, no necesariamente se anticipa que el problema desaparezca debido a que muchos casos no son causados por hepatitis AAH positiva. Gocke (17) ha estimado que se podría reducir la frecuencia de hepatitis por 25 por ciento eliminando todos los donantes AAH positivos pero todavía se necesita información más definitiva al respecto.

Alrededor de 2-3 millones de donaciones de sangre

ocurrieron en los Estados Unidos en 1971 (20). Aproximadamente 12,500 personas con prueba AAH positiva fueron rechazadas. Ya hemos comentado sobre el significado para el recipiente de recibir sangre positiva. Ahora, ¿qué representa para el donante tener su sangre positiva?

Aparte de ser portador del virus de la hepatitis y por lo tanto, ser excluido como donante de sangre debido a su alto potencial de transmitir la enfermedad al recipiente de su sangre, la presencia del AAH representa una variedad de implicaciones clínicas.

Banke (21) no encontró evidencia de enfermedad hepática en 17 donantes positivos estudiados en Copenhagen incluyendo biopsias hepáticas. Kliman (22) encontró anomalías en la función hepática en una tercera parte de los 114 donantes positivos estudiados en Massachusetts. Por el contrario, Singleton (23) detectó evidencia de enfermedad hepática, variando desde cambios mínimos hasta hepatitis crónica, en 22 de 25 casos estudiados en Denver.

Estos resultados indican que la incidencia de enfermedad hepática en donantes AAH positivos es variable y se necesitan estudios más detallados y extensos para definirla.

b) Inmunización

En esta área de la prevención y conquista de la hepatitis como problema de salud pública mundial parece haber la esperanza de grandes logros.

Los estudios de Krugman (24) en N. Y. revelan que una preparación inactiva de suero con AAH positivo puede inducir una respuesta de anticuerpos y prevenir el desarrollo de la hepatitis. Este método permite eliminar el potencial infeccioso del virus pero reteniendo su antigenicidad cuando se hierve el suero conteniendo el AAH a 98°C por un minuto. Esta forma de vacunación activa ha sido utilizada en los niños retardados mentales de Willowbrook con resultados prometedores.

Prince (25, 26) ha conseguido una preparación de gamma globulina especial con un alto título de anticuerpo contra AAH que es alrededor de 50,000-100,000 veces mayor que el de la gamma globulina usada regularmente en la prevención o modificación de la hepatitis viral infecciosa MS1. La administración de esta preparación obtenida del suero de pacientes hemofílicos multi-transfundidos, confirió inmunidad pasiva en el 70 por ciento de los pacientes estudiados por Krugman (27). Estos estudios demuestran otro gran avance en el campo del Antígeno Australiano y su efectividad parece añadir más certeza a la prevención futura de la hepatitis MS2, hasta ahora con resultados más o menos inefectivos

mediante el uso de la gamma globulina regular.

5. Valor Etiológico

La presencia del AAH en el suero de pacientes con enfermedad hepática ha sido investigada. En pacientes con hepatitis crónica su frecuencia promedio es de 18.4 por ciento, mientras que en pacientes con cirrosis es de 9.5 por ciento. Sin embargo, las variaciones en series individuales fluctúan entre 0 y 67 por ciento (7). El rol etiológico de la hepatitis viral en las enfermedades hepáticas crónicas ha sido objeto de innumerables controversias. Aunque la mayoría de los pacientes con hepatitis viral recuperan totalmente no hay duda que algunos progresan a la fase crónica. Esta relación parece ser más probable en la hepatitis MS2 especialmente en los pacientes que se convierten en portadores persistentes del AAH y en las formas anictéricas de la enfermedad.

El carcinoma hepatocelular, que ocurre más frecuentemente asociado a la cirrosis, especialmente del tipo post-necrótica o post-hepatítica también ha demostrado una alta frecuencia de positividad para el AAH que fluctúa entre 0-42 por ciento. Estos resultados fortalecen la relación hepatitis-cirrosis-hepatoma y ha llevado a algunos investigadores a postular que la hepatitis viral sea una condición pre-cancerosa.

La transmisión maternal-fetal de los virus de rubela, enfermedad citomegálica y herpes simplex ha sido documentada y es posible que similarmente pueda ocurrir con el de la hepatitis. Esto podría ser importante en la patogénesis de la hepatitis neonatal.

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CIRUGIA RADICAL PARA TRAUMA SEVERO DEL HIGADO Y PULMÓN

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Nuestra sociedad demuestra una tendencia innegable de violencia; a veces producto de choques, algunos de personalidad, otras de ideologías, las más, de vehículos de motor. Son los cirujanos quienes casi siempre deberán tratar los resultados, y es esencial que se esté preparado para pacientes con trauma severo. Informamos un caso tratado quirúrgicamente, donde fue necesario hepatectomía derecha y segmentectomía del lóbulo inferior del pulmón derecho, además de tratamiento intenso médico, para lograr un resultado exitoso.

Informe del Caso

E. N. R., joven estudiante de 18 años, fue admitido de emergencia al Hospital Auxilio Mutuo, el 11 de marzo de 1971, poco después de ser herido de bala durante los disturbios de ese día en el Campus Universitario de Río Piedras.

El orificio de entrada se encontró en el área subcostal derecha, sin orificio de salida. Exangüe, su tensión arterial era de 90/60 y pulso de 140. El historial anterior reveló sólo asma. El abdomen estaba en tabla y la placa de pecho reveló hemotorax inmediatamente tratado por tubo intercostal.

Fue explorado por abordaje toraco abdominal. La bala perforó el lóbulo derecho del hígado, pasó el diafragma, traspasó el lóbulo inferior del pulmón derecho y se alojó en la pared torácica posterior después de fracturar la undécima costilla. Ante nuestros mismos ojos, desarrolló un hematoma subcapsular masivo, lo cual forzó una hepatectomía derecha clásica. Se ligó individualmente la arteria cística, hepática derecha, vena porta derecha y ducto hepático derecho, según la técnica de Quattlebaum (1), y logrado el control vascular, pudo fracturarse manualmente el parénquima hepático como recomienda Lin (2), con ligadura de ductos biliares y vasos sanguíneos según necesario, todo a través del lecho de la vesícula.

Por continuar la pérdida de sangre del parénquima pulmonar lacerado y destruido, éste se extirpó por medio de una segmentectomía lateral, y se preservó el máximo de parénquima pulmonar posible. Se introdujo un tubo en T al sistema biliar.

El procedimiento hizo necesaria la autotransfusión, después de filtrar la sangre aspirada durante la operación, porque

la situación de emergencia, tanto en la sala de operaciones como en la comunidad, impidió obtener sangre de otra forma.

El curso postoperatorio fue tormentoso, aunque las funciones hepáticas se mantuvieron en forma admirable. Tuvo reemplazo con líquidos y sangre según la variación en la tensión venosa central, y recibió apoyo mecánico respiratorio con respirador de volumen, además de broncodilatadores, albumina, staphcillin, Keflin, penicilina, gammaglobulina, Vitamina K y un curso breve de Amicar.

El esputo, purulento y a veces teñido de sangre inmediatamente post cirugía se normalizó 4 días después. Tres días después de la operación comenzó diuresis con gravedad específica de 1.005, probablemente secundaria a necrosis tubular, con la fase anúrica abortada por manitol administrado en sala de operaciones.

Durante estos primeros días su cuadro hematológico estuvo estable, y las posibles complicaciones de fibrinólisis y coagulación intravascular diseminada no ocurrieron. Su tiempo de protrombina se alargó ligeramente y, en promedio, las plaquetas fueron 110,000. Sin evidencia de fibrinólisis, el Amicar fue discontinuado 24 horas después de cirugía. Su creatinina estuvo en 0.87 y BUN 37 al momento de diuresis.

La temperatura no bajó de 38°C durante la primera semana, con conteo de blancos de 17,000.

En placa de pecho tomada el 18 de marzo se detectó aire bajo el diafragma (Figura 1). Substituímos Keflin por Dinapen y Garamicina, por haberse normalizado la situación renal. La fiebre cedió, y con control diario radiográfico se comprobó la disminución progresiva hasta desaparecer del aire subdiafragmático.

Para 3/21 el conteo de blancos regresó a normal y poco después se discontinuaron todos los antibióticos.

Reapareció la fiebre 3 semanas después de cirugía. Colangiograma por el tubo en T no reveló absceso, y se retiró el tubo (Figura 2). Las pruebas de laboratorio demostraron un aumento en gama globulina (47 por ciento). Toracentesis fueron negativas. Administramos Keflin y Kantrex y las pruebas séricas y de orina fueron negativas para infección viral. Gamagrafía hepática en 4/14 mostró buena captación y esplenomegalia. La prueba de antígeno australiano fue negativa el 4/19. Poco después, cedió la fiebre, y se dió de alta en dinapen, el 4/21. Desde entonces, ha progresado bien y actualmente no tiene síntomas y está trabajando, sin problemas.

Discusión

La primera lobectomía parcial hepática la informó Langenbuch en 1888, sin embargo, intervenciones radicales hepáticas con buenos resultados son de época más



Fig. 1: Radiografía que muestra colección de aire bajo el diafragma muy sugestivo de absceso subdiafragmático. Desapareció, tratado con antibióticos.



Fig. 2: Colangioma efectuado por el tubo en T muestra sistema biliar del lóbulo izquierdo. La fractura de la undécima costilla, con fragmentos de bala, es evidente.

reciente (3). Para 1887 podían describirse series clínicas de trauma hepático donde la mortalidad sin cirugía era de 67 por ciento y para la Primera Guerra Mundial, aún con cirugía, la mortalidad fue 66 por ciento, sin mejorar grandemente en años subsiguientes. Durante la Segunda Guerra Mundial pudo disminuirse esta mortalidad a 27 por ciento y Sparkman logró bajarla aún más, a 10 por ciento, en 1954 (4, 5).

Extirpaciones masivas de parénquima hepático ya son más frecuentes, McClelland y Shires (6) informaron una mortalidad de 20 por ciento en 25 pacientes, mientras Blasegarani (7) logró que de 11 pacientes operados 10 sobrevivieran.

Dado el caso nuestro, donde trauma es una causa importante de mortalidad, y al ser trauma hepático difícil de tratar adecuadamente, creemos oportuno discutir este caso brevemente.

Primero, sutura primaria de laceraciones sencillas hepáticas, con drenaje, es lo más común e indicado. Para trauma extenso la extirpación lobar, o segmentaria, es preferible al ataponamiento con gaza, al evitar las complicaciones de hemorragias repetidas, infección y hematóbilia. La mortalidad final depende de otros sistemas traumatizados según se describe en el excelente libro de Madding y Kennedy (8), pero valga señalar que cuando se trata de intervenciones radicales electivas para carcinoma primario hepático, Dillard (9), logró una mortalidad de 8 por ciento y una sobrevida a 5 años de 50 por ciento.

Recientemente, Pinkerton y sus colegas (10) describieron detalladamente el curso postoperatorio de 31 pacientes con extirpaciones masivas hepáticas, donde por lo menos se sacó un lóbulo. En 19, la razón fue trauma. De todos los pacientes, la mitad tuvo un

período postoperatorio sin complicaciones, pero 16 pacientes experimentaron 34 complicaciones distintas. Similar a nuestro caso, en 14 pacientes apareció una fiebre en exceso a 38.8°C cuya causa nunca se determinó. En nuestro paciente su primer curso febril puede atribuirse a un pequeño absceso subdiafrágico, sin embargo, aunque sospechamos etiología viral para el segundo episodio, nunca se pudo comprobar.

No debe temerse a la insuficiencia hepática después de lobectomía hepática siempre y cuando el parénquima remanente sea normal y los vasos y ductos queden intactos. Los cambios bioquímicos y hematológicos son bien conocidos (10): (1) la azúcar en sangre disminuye (aunque generalmente pasa desapercibido por las infusiones de suero), (2) la albumina baja, para lo cual se recomienda administración de albumina sérica, (3) las enzimas se alteran, con elevación del SGOT, SLDH, SGPT, acompañada por cambios similares de la fosfatasa alcalina y la bilirubina; el colesterol y los triglicéridos disminuyen, (4) la protrombina puede prolongarse después de cirugía pero usualmente retorna a valores normales en 7 a 10 días, y se ha detectado disminución en fibrinógeno, factores V, VII, IX, X y plasminógeno.

Aunque se recomienda la Vitamina K para tratamiento postoperatorio, cualquier terapia debe basarse en estudios de coagulación. Las causas más comunes de hemorragia tardía son fibrinolisinias o coagulopatía por consumo.

Decompresión biliar profiláctica es ahora un tema de controversia. Hay quienes la recomiendan, otros se oponen, especialmente en niños. De cualquier manera puede ser un factor en un problema serio que acompaña con singular frecuencia este tipo de cirugía: la hemorragia gastrointestinal postoperatoria debido a úlcera. Los antácidos deben administrarse profilácticamente a estos pacientes.

Es conocido ya la capacidad del hígado para regenerarse. La gamagrafía (Figura 3) de nuestro paciente muestra lo acontecido en un mes después del trauma. Actualmente, el joven está asintomático, ha crecido, y trabaja, sin problemas.

Resumen

Se informa el curso clínico de un paciente con trauma masivo al hígado y pulmón, tratado exitosamente con extirpación del lóbulo hepático derecho y segmentectomía lateral del lóbulo inferior del pulmón derecho. Esta cirugía radical puede llevarse a cabo con una mortalidad baja y es responsabilidad de todo cirujano llamado a tratar trauma de familiarizarse con la técnica quirúrgica y con las complicaciones posibles post cirugía.



Fig. 3 (a, b): Gamagrafía del hígado y bazo un mes más tarde. El tamaño hepático es verdaderamente sorprendente.

Summary

A case of severe hepatic and pulmonary trauma is presented, treated successfully with right hepatic lobectomy and pulmonary segmentectomy. This radical surgery can have a low mortality and it is the responsibility of all surgeons treating trauma to acquaint themselves with the technique involved and the possible postoperative complications.

Reconocimiento

Contribuyeron en forma muy valiosa al tratamiento de este paciente los doctores Jorge Báez, Hugo Montes, Heriberto Morales, y E. Vélez García. Agradecemos sus esfuerzos a todo el personal de enfermería y paramédico del Hospital Auxilio Mutuo, y en especial al personal de la sala de cuidado intensivo.

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HEPATITIS VIRAL: CONCEPTOS ACTUALES SOBRE ETIOLOGIA Y EL ANTIGENO ASOCIADO A HEPATITIS (AUSTRALIANO)

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La hepatitis viral es una enfermedad común en nuestro ambiente. Descrita por Hipócrates bajo el nombre de ictericia epidémica (1), ha acompañado al hombre occidental a través de la historia de nuestra cultura. De Hipócrates al 1940 el estudio de la enfermedad fue esencialmente descriptivo y el progreso en su conocimiento, lento. Los últimos treinta años se han caracterizado por un aumento explosivo en la investigación con la culminación en el descubrimiento en 1964 de un antígeno íntimamente asociado a la hepatitis (3). Presentamos aquí los conceptos actuales sobre etiología e inmunología, enfatizando aquellos adelantos recientes que por su importancia clínica permiten al médico en práctica combatir con mayor efectividad el problema de la hepatitis.

Hepatitis.... ¿Viral?

El carácter epidémico conocido de la hepatitis, sugiere una etiología infecciosa para la enfermedad. En el 1941 se demostró por primera vez que la enfermedad podía ser transmitida experimentalmente de humanos enfermos a voluntarios humanos sanos (2). La transmisión a voluntarios humanos sanos ha probado ser la técnica fundamental para estudiar la enfermedad bajo condiciones experimentales controladas y ha contribuido información valiosa sobre la etiología de la hepatitis. La evidencia que hoy tenemos en favor de una etiología infecciosa-viral puede resumirse en las siguientes observaciones:

1. La hepatitis puede ser endémica u ocurrir en brotes epidémicos (4).
2. La enfermedad es transmisible a través de las secreciones, excreta y sangre del enfermo (5, 6).
3. El material infeccioso no pierde su infectividad al pasar por un filtro bacteriológico (7).
4. Existe un período de incubación entre la inoculación de un voluntario y el comienzo de los síntomas (8).
5. Un ataque de hepatitis induce inmunidad contra ataques subsiguientes (9).
6. La hepatitis epidémica puede ser prevenida administrando gamma globulina a los sujetos ex-

puestos (10).

Estos datos constituyen evidencia positiva en favor de una etiología infecciosa-viral para la hepatitis y se resumen en la Tabla I. Además existe el dato negativo; al presente no existe evidencia alguna que indique que la hepatitis no es una enfermedad viral. Es obvio, sin embargo, que toda la evidencia es indirecta y aunque sugiere que la enfermedad es viral no prueba que lo sea.

A pesar de múltiples intentos por los mejores laboratorios virológicos del mundo no ha sido posible aislar el virus de la hepatitis (11). Tampoco el microscopio electrónico ha podido demostrar la presencia de un virus en las lesiones hepáticas (12). Es evidente que no se han cumplido los postulados de Koch y la etiología viral en hepatitis aunque generalmente aceptada y probablemente correcta hasta el presente no ha sido probada.

Hepatitis - Caracterización en Tipos

Desde los primeros estudios llevados a cabo en voluntarios se hizo evidente que existía más de un tipo de hepatitis (5, 6, 9). Estudios ulteriores han confirmado que existen por lo menos dos tipos de hepatitis (13) que pueden ser identificados en términos de su epidemiología, período de incubación, pronóstico y otras características que se resumen en la Tabla II. Es importante señalar varios puntos prácticos. Primero, cada tipo ha recibido diferentes nombres de acuerdo a la característica que cada autor considerara más importante y esto ha causado cierta confusión en la literatura. Segundo, el concepto conocido de que la hepatitis sérica se transmite por vía parenteral exclusivamente (5, 9) es probablemente erró-

**TABLA I: HEPATITIS COMO ENFERMEDAD
VIRAL: CARACTERISTICAS**

Epidémica
Trasmisible
Agente Filtrable
Período Incubación
Produce Inmunidad
Prevenible con Gamma Globulina

TABLA II: TIPOS DE HEPATITIS

Características	Tipo I	Tipo II
Período incubación (semanas)	2-6	4-26
Epidemiología	Epidémica	Esporádica
Transmisión Fecal-Oral	Sí	Sí
Transmisión Parenteral	Sí	Sí
Inmunidad Adquirida	Al Tipo I	Al Tipo II
Protección por G-Globulina	Eficaz	Dudosa
Mortalidad	Baja (1/1000)	Alta (10/100)
Evolución a Enfermedad Crónica	Rara	Frecuente
Antígeno Asociado a Hepatitis	Negativo	Positivo
Nombres	Hepatitis infecciosa	Hepatitis sérica
	Hepatitis epidémica	Hepatitis esporádica
	Hepatitis IH	Hepatitis SH
	Hepatitis incubación corta	Hepatitis incubación larga
	Virus A	Virus B
	MS-I	MS II
	AAH negativo	AAH positivo

neo. Evidencia obtenida recientemente demuestra que la hepatitis tipo II puede transmitirse por vía fecal-oral (13). Tercero, la hepatitis tipo II es una enfermedad peligrosa con mayor morbilidad y mortalidad en la fase aguda (14) y con mayor riesgo de desarrollar secuelas crónicas (15). Finalmente, muchas veces en la práctica no es posible distinguir un tipo del otro, particularmente cuando no existe un historial de transfusión o inyección que nos permita estimar el período de incubación. A este fin la determinación del Antígeno Asociado a la Hepatitis (AAH) puede ser de gran utilidad ya que de ser positiva identifica la enfermedad como tipo II.

Antígeno Asociado a Hepatitis (AAH) o Antígeno Australiano (AU1)

El descubrimiento de antígeno asociado a la hepatitis (AAH) fue producto, como otros descubrimientos en medicina, de una observación incidental hecha por un investigador alerta. En 1964 Blumberg y colaboradores, investigando las precipitinas de B-lipoproteínas, observaron que al mezclar suero de un aborigen australiano con suero de un hemofílico que había recibido múltiples transfusiones ocurría una precipitina que no se ajustaba a las características conocidas para precipitinas de B-lipoproteína. En honor al proveedor nombraron el nuevo antígeno Australiano (3). En el 1966 estudiando la prevalencia del Antígeno Australiano en una institución dedicada al cuidado de pacientes con síndrome de Down (Mongolismo) se

descubrió una relación entre el antígeno y la hepatitis (16). Un año más tarde esta relación se delimitó aún más al descubrirse que el antígeno se asocia con la hepatitis Tipo II (17, 18) y no con el Tipo I (19) (Tabla II).

Relación entre Antígeno AAH y la Hepatitis

La asociación estrecha entre el antígeno y la hepatitis Tipo II (17, 18) (Tabla II), descubierta hace solo cinco años, ha sido estudiada por diversas disciplinas. Estos estudios han proporcionado sólido respaldo al concepto de un antígeno asociado a hepatitis (20) y se resumen a continuación:

Estudios Estadísticos (19, 21, 22) - La evidencia estadística para una relación entre el antígeno y la hepatitis se resume en la Tabla III. La prevalencia del antígeno es alta en la hepatitis tipo II y en aquellas enfermedades que se consideran secuelas de la hepatitis, mientras que es baja en la población norteamericana "normal" e inexistente en la hepatitis tipo I y en enfermedades hepáticas no asociadas con hepatitis.

Estudios Epidemiológicos - El antígeno se comporta como un agente infeccioso ya que puede ser adquirido por personas que tenían una reacción previa negativa (17). Además, sangre o plasma AAH positiva produce hepatitis aguda AAH positiva en las personas que la reciben (21). La cantidad de sangre AAH positiva necesaria para transmitir hepatitis es tan pequeña que puede pasar desapercibida. Se ha demostrado que aún la san-

gre con título de AAH bajos se mantiene infectiva al diluirse diez millones de veces (21), lo que plantea la posibilidad de que pequeñas abrasiones con instrumentos contaminados inadvertidamente (navajas de barbero, instrumentos dentales, etc.) o picadas de mosquitos sean importantes en la transmisión de la enfermedad. También se ha demostrado que la ingestión oral de material conteniendo al antígeno en altas concentraciones produce hepatitis en individuos susceptibles (13).

Estudios Clínicos - El antígeno aparece temprano en el período de incubación de la enfermedad, persiste por un tiempo variable y desaparece en la mayoría de los pacientes durante la fase clínica al momento que suben los niveles de anticuerpos anti AAH (17, 23, 24). En algunos pacientes el antígeno persiste indefinidamente (23, 24), por razones desconocidas; unos enfatizan los factores asociados con el huésped y postulan un defecto genético manifestado por una susceptibilidad anormal a la infección (25); otros enfatizan factores externos como la contaminación fecal del ambiente, la cantidad de virus recibida y la agresividad del virus (20). La persistencia del antígeno no afecta el pronóstico inmediato; los pacientes con antígeno persistentemente positivo mejoran de su hepatitis aguda al mismo ritmo que aquellos en que el antígeno desaparece (23, 24). El pronóstico a largo plazo es diferente, teniendo los pacientes con antígeno persistentemente positivo un riesgo mayor de desarrollar enfermedad crónica (15, 22).

Estudios patológicos - Pacientes con hepatitis viral aguda AAH positiva demuestran fluorescencia en sus células hepáticas cuando éstas se exponen a anticuerpo anti AAH utilizando técnicas histoimmunofluorescentes (26). Esto se ha aducido como evidencia en favor de la presencia del antígeno en las células hepáticas durante la fase aguda de la enfermedad.

Estudios Básicos - El antígeno AAH es de naturaleza protéica (27), su forma y tamaño corresponde a la que se postula para el virus de la hepatitis (28) y su resistencia a agentes físicos y químicos es similar a la del agente causal de la hepatitis (29).

Los estudios presentados sugieren la posibilidad de que el AAH sea el virus de la hepatitis. Esta posibilidad no puede ser aceptada todavía, ya que no existe ninguna evidencia directa en su favor. Estudios de la estructura del AAH no han podido demostrar que contenga ácidos nucleicos y sugieren que sea una proteína no infecciosa asociada a la capa del virus (23). Es posible que el AAH no represente el agente causal de la hepatitis sino una proteína producto de la necrosis hepatocelular. Este postulado puede explicar la mayor parte de las observaciones arriba mencionadas y aunque poco favorecido

no ha sido descartado todavía (30).

Resumen - Las observaciones hechas en los últimos cinco años demuestran fuera de toda duda que el antígeno originalmente denominado Antígeno Australiano está íntimamente relacionado con la hepatitis tipo II (Tabla II). La naturaleza del antígeno y su significado biológico quedan por delucidarse. En tanto esto se haga, se considera más correcto el nombre de antígeno asociado a la hepatitis (AAH).

Aplicación Práctica de la Determinación de AAH

Aparte de su importancia para el investigador, la determinación del AAH ha probado tener gran importancia práctica en el diagnóstico, pronóstico y prevención de la hepatitis. Debe interpretarse bien, aunque un AAH positivo tiene gran valor, lo opuesto no es necesariamente cierto. Una determinación de AAH negativa no establece que el paciente sea AAH negativo. La razón para esta discrepancia estriba en los métodos usados. El método de inmunodifusión en placas de agar (Ouchterlony) usado en la mayoría de los laboratorios es sencillo y fácil pero poco sensitivo, estimándose que solo detecta un 20-40 por ciento de los casos AAH positivos (20). Los métodos basados en reacciones de fijación de complemento, mucho más sensitivos que las placas de Ouchterlony, tienen la desventaja de ser técnicamente complejos y no está en uso general todavía. El informe de un AAH negativo (Ouchterlony) no tiene ningún significado por sí solo y debe interpretarse a la luz de los hallazgos clínicos y epidemiológicos.

Revisemos ahora las aplicaciones prácticas de la prueba en el diagnóstico, pronóstico y prevención de la hepatitis.

Diagnóstico: Un AAH positivo puede tener valor diagnóstico en las siguientes situaciones:

1. Diagnóstico temprano de hepatitis en personas que se mantienen bajo vigilancia periódica por tener un riesgo ocupacional alto (31): personal de hemodiálisis, técnicos que trabajan con sangre, cirujanos, etc. La prueba se hace positiva en el período de incubación, antes de que la enfermedad se manifieste. En esta situación la determinación tiene importancia pronóstica y terapéutica ya que la severidad de la enfermedad depende entre otras cosas de la cantidad de virus recibido. Remover el paciente del ambiente contaminado antes de que reciba una cantidad masiva del agente infeccioso puede ser importante. Además aunque el valor terapéutico del descanso en cama durante la fase clínica de la

hepatitis es incierto (32, 33), no hay información sobre el valor del descanso en cama cuando se instituye durante el período de incubación de la enfermedad y es posible que resulte beneficioso.

2. Diagnóstico del tipo de hepatitis - La determinación de un AAH positivo identifica la hepatitis como tipo II. Debido al aumento reciente en el uso de drogas inyectables y la alta prevalencia de hepatitis tipo II en los adictos (34), es frecuente sospechar adicción o uso de heroína en el paciente joven con hepatitis AAH positiva que no tiene historial de transfusiones de sangre o inyecciones terapéuticas. En esta situación es necesario proceder con cautela ya que la hepatitis AAH positiva puede ser transmitida por vía fecal-oral (13), además es muy posible que también sea transmitida por instrumentos de barbería, instrumentos dentales, picadas de mosquito (35), etc. La hepatitis AAH positiva por sí sola no constituye evidencia de uso ilegal de drogas.

3. Detección de enfermedad hepática crónica asintomática - El 0.1 por ciento de la población norteamericana "normal" es AAH positiva (Tabla III) definiéndose como "normal" personas que no presentan evidencia de enfermedad hepática.

Estudios recientes indican que no es raro encontrar evidencia histológica de enfermedad hepática en casos asintomáticos AAH positivos (36).

4. Diagnóstico etiológico en casos de enfermedad hepática de origen oscuro - La determinación de AAH positivo en estos casos los identifica como hepatitis viral tipo II o alguna de sus secuelas crónicas.

5. Diagnóstico de hepatitis anictérica.

6. Evaluación de casos con elevación persistente de transaminasas y ninguna otra evidencia de enfermedad.

7. Diagnóstico diferencial de ictericia.

Pronóstico: La hepatitis AAH positiva es una enfermedad severa con una morbilidad y mortalidad significativa y un riesgo elevado de desarrollar secuelas crónicas, particularmente aquellos pacientes en que el antígeno persiste positivo (22, 23, 24).

Prevención: La determinación de AAH cobrará su mayor importancia en la prevención de la hepatitis:

1. Todo Banco de Sangre debe descartar la sangre o plasma AAH positivo. Todo donante debe ser probado para AAH y en caso de ser positivo, eliminando como donante (37). Se calcula que la aplicación rutinaria de esta medida por todos los Bancos de Sangre de los Estados Unidos evitará en un solo año 50,000 casos de hepatitis y 1,000 muertes (38).

2. Aunque la gamma globulina inmune ha probado ser efectiva en la prevención de la hepatitis tipo I (10), su efectividad en la prevención de la hepatitis tipo II

TABLA III: PREVALENCIA DEL AAH

Población Norteamericana "normal"	0.1 por ciento
Hepatitis Aguda Tipo II	93 por ciento
Hepatitis Aguda Tipo II	0 por ciento
Hepatitis crónica	10-70 por ciento
Cirrosis Posthepatítica	6-25 por ciento
Hepatoma	5-40 por ciento
Cirrosis biliar primaria	0 por ciento
Ictericias Obstructiva	0 por ciento
Hepatitis medicamentosa	0 por ciento
Cirrosis del alcohólico	0 por ciento

queda por demostrarse. La administración rutinaria de gamma globulina a los contactos de pacientes con hepatitis AAH positiva y a pacientes que reciben transfusiones de sangre es controversial y continúa bajo estudio (39).

3. Detección del AAH entre personas asintomáticas que están en situación de transmitir la enfermedad (cirujanos, dentistas, barberos, cocineros, etc.). Estas personas pueden ser portadores asintomáticos de la enfermedad y su manejo plantea serios problemas éticos, sociales y económicos. La complejidad de estos problemas no permite su discusión en esta presentación. Para una opinión el lector interesado debe referirse al artículo por Chalmers y Alter (38).

Perspectivas Futuras: La prueba de AAH debe ser ya parte de la evaluación rutinaria de los donantes de sangre (37) y es concebible que se convierta en una prueba rutinaria como las pruebas serológicas de sífilis que nos ayude a entender mejor y controlar la epidemiología de la hepatitis. El estímulo que el AAH ha dado al estudio de la hepatitis sin duda cambiara la enfermedad como la conocemos hoy y levanta la posibilidad de que puedan desarrollarse antisueros específicos para el tratamiento y prevención de la enfermedad así como vacunas efectivas. Podemos esperar con cauteloso optimismo que la hepatitis viral, hoy un problema médico y de salud pública de grandes proporciones, siga la evolución histórica de otros azotes de la humanidad y se controle al punto de convertirse en una curiosidad clínica.

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HYPERBILIRUBINEMIA NOT DUE TO HEMOLYTIC DISEASE OF NEWBORN

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Neonatal jaundice is a diagnostic problem of frequent incidence. The Pediatrician is faced with a wide variety of possible etiologic factors. Our chief concern is with hyperbilirubinemia due to an elevation of the indirect bilirubin, that is water insoluble but lipid soluble. Due to this solubility the toxic accumulation in brain tissue leads to encephalopathy or kernicterus.

In this problem of hyperbilirubinemia we have to consider that the common denominator of all neonatal jaundice is the limited capacity of the newborn liver to convert bilirubin to the soluble pigment of bilirubin diglucuronide. There is a daily degradation of 0.5 gm of hemoglobin yielding 17 mg. Bilirubin. This constitutes the physiological load to be handled by the newborn liver. The difference in the rate of formation and excretion of bilirubin remains constant. The bulk of bilirubin accumulates initially in the plasma. After 2 days of age more bilirubin goes into adipose tissue and the serum concentration decreases. On the third day bilirubin begins to appear in central nervous tissue and simultaneously the slopes of serum and adipose tissue decreases. The accumulation of toxic levels of bilirubin Indirect in brain tissue leads to Encephalopathy or kernicterus.

Clinical Material

This study was carried out in the Newborn Service of the San Juan City Hospital during October 1, 1961 to July 31, 1963 in order to investigate the causes of neonatal jaundice in our milieu.

Methods

In our Maternity Service of the San Juan City Hospital we had around 500-600 deliveries per month. Due to the

limited number of beds the mothers with their babies without any neonatal complication were discharged during first 24-48 hours. Only the small babies under 4 pounds or with clinical complications stayed longer time. Instructions were given to the mother to bring their babies to the Outpatient Department during the second to third day or sooner if they were jaundiced.

The babies' red cells were studied to determine the presence of antibodies with specific test to diagnose ABO incompatibility and the maternal blood was tested with the baby's red cells ABO compatible to eliminate the possibility of erythroblastosis due to a sub-group incompatibility.

Pathological icterus was considered according to the following criteria:

- 1) Icterus precox = jaundice visible during first 24 hours or if the bilirubin level was 10 mg percent or more.
- 2) Daily Increase in Serum bilirubin level of 5mg percent or more.
- 3) An Increase in the total level of bilirubin above the physiological basis established in our hospital, that is 13 mg percent for the full term and 16 mg percent for the premature baby.
- 4) Prolonged jaundice in the full term if icterus above 2 mg. persisted after 1 week old and in the premature if jaundice was of two weeks or more duration.
- 5) Values of Direct Bilirubin above 0.5 mg percent to be considered as possible hepatocellular damage.

Our neonatal statistics revealed an average of 500-600 deliveries per month with an incidence of 10 percent prematures or small for date babies. In our group physiological jaundice was below 50 percent probably because mothers did not bring mild cases of jaundice to medical attention and or because examining physician considered the cases too mild to be worthwhile to have laboratory determinations.

Pathological Icterus was divided in:

- 1) Hyperbilirubinemia due to hemolytic disease of newborn ABO, Rh, subgroups incompatibility or Enzymatic factors.
- 2) Hyperbilirubinemia not due to Hemolytic Disease.
- 3) Hyperbilirubinemia of undetermined Etiology. The group that we are going to present in this discussion is Hyperbilirubinemia not due to Hemolytic disease.

Hyperbilirubinemia not Due to Hemolytic Disease of the Newborn

In the present study 76 cases of hyperbilirubinemia not explained by hemolytic processes as ABO or RH incompatibility were investigated. Among the cases

From the Newborn Service San Juan City Hospital, Puerto Rico Medical Center. Investigation supported by Public Health Service N. I. H. Grant No. 6467. Chief Investigator: Dra. Mercedes Torregrosa; Co-investigators: Dra. Eloísa Muñoz de Carrascal y Dr. Egidio Colón Rivera. Accepted for presentation at the II Latin American, IX Pan American and IX Colombian Pediatric Congresses July 25, 1970, Bogotá, Colombia.

studied it was found that 35 of these had respiratory distress; 23 were due to sepsis; 6 cases were associated with cyanosis; during first twenty four hours, 6 more developed cephalohematoma with jaundice and the other 6 had miscellaneous causes to account for the hyperbilirubinemia. Among the miscellaneous cases three were from a luetic mother, one from a diabetic mother, one had inspissated bile syndrome and the other developed petechiae of the scalp.

In the group of 35 who developed *respiratory distress* with jaundice we had 21 full terms and of these one was delivered by cesarean section from a diabetic mother. The baby developed hayline membrane radiologically confirmed. In Table I there is an analysis of the cases with respiratory distress.

TABLE I: RESPIRATORY DISTRESS (35)

1. 21 Full terms, 14 prematures.
2. Onset of jaundice - majority 2 rd. - 3rd. day
3. Total bil. above 20 mg. percent-13 (8 Ft, 5 prem)
4. Direct Bil. above 0.5 mg percent-15 (3 prem, 12 Ft)
5. Exchange T. -2 (1 prem., Twice; 1 Ft)
6. Mortality 0
7. Mech. Producing Jaundice: (4) Bibliography
 - a. Hypoglycemia
 - b. Respiratory acidosis-altering albumin binding capacity.
 - c. Hypoxia-hepatocellular damage.

In the majority of the cases the onset of jaundice was during the second to third day of life. Levels of bilirubin above 20 mg. percent were attained in 13 infants (8 Ft) and 5 were prematures. Fifteen babies (3 prem. and 12 Ft) had a direct bilirubin above 0.5 mg. percent Exchange transfusions were performed in two cases. One premature with a total bilirubin of 22 mg percent at onset, rising up to 27 mg percent of bilirubin, prior to exchange required two transfusions. The other baby who had also an exchange transfusion was a full term with a total bilirubin of 27 mg percent at the onset of jaundice. No death was registered in the group.

The explanation for the production of jaundice in respiratory distress is based on various mechanisms. One contributing factor is the hypoglycemia which is a metabolic factor leading to depletion of carbohydrate. With a decrease source of glucose we have a diminished production of glucuronic acid. Glucose is a precursor of glucuronic acid. One alcoholic group of glucose is oxidized and glucuronic acid is produced. (2) In the liver microsome glucuronic acid is conjugated with bilirubin in the presence of glucuronyl transferase.

Delayed feeding in babies with respiratory distress may increase the fraction of serum non sterified fatty acids which can compete with bilirubin for albumin binding (4) sites, thus aggravating the hyperbilirubinemia. In prematures with respiratory distress and inrespiratory acidosis there is an altered albumin binding capacity of bilirubin. One mole of albumin binds two moles of bilirubin i.e., 1 gram of albumin binds 15 mg. of bilirubin at ph 7.4 (2).

Infants with hypoxia are predisposed to have hepatocellular damage with a delay in the excretion of diglucuronide, which is the conjugation form of bilirubin. With hypoxia there is a decrease in the albumin binding capacity due to changes in ph and there is an altered permeability of blood-brain barrier with increased cell susceptibility to toxic effects of bilirubin.

In the group of 23 infants with sepsis associated with hyperbilirubinemia, 14 were full terms and 9 were prematures. See Table II.

Three of the prematures died. One of them was an infant born from a diabetic mother delivered by cesarean section. This infant had a positive blood culture with pseudomona in the blood culture and associated respiratory distress. The other death was due to sepsis not confirmed bacteriologically.

In Table II we have that the onset of jaundice in the majority of cases was during the second to third day of life.

TABLE II: SEPSIS (23)

1. 14 Ft. 9 Prem. (3 deaths: 2 Pseudomonas and 1 Clinical Sepsis.
 2. Onset of jaundice- majority 2nd. 3rd day
 3. Total bil. above 20 mg. percent 7 (5 Prem., 2 Ft.)
 4. Direct bil. 0.5 mg. percent 12 (8 Ft, 4 Prem)
 5. Exchange transf. 1 Ft. (with 25 mg. percent of bil)
 6. Etiology: 10 staph coag positive
 7. Mechs. producing jaundice:
 - a. Hemolysis
 - b. Hepatotoxic factor
- 2 E. Coli
1 Klebsiella

In these series of cases levels of bilirubin above 20 mg. percent were attained in 7 infants (2 Ft and 5 Prem.). It is noteworthy to remark that prematures may have an elevation of partial conjugated bilirubin in the form of monoglucuronide. The monoglucuronide fraction though it gives an indirect reaction is less toxic than the unconjugated indirect bilirubin per se. This explains why some prematures may show an elevated indirect bilirubin above 20 percent without manifest-

ing signs of kernicterus. Newborn infants with bacterial infections showed elevation of bilirubin monoglucuronide. Almost invariably these were *Escherichia coli* infections and *E. Coli* is known to cause a bacterial-type hepatitis (2).

In 9 infants (5 full term and 4 prem) the direct bilirubin was above 0.5 mg percent it is known that with sepsis there may be hepatocellular damage subsequently affecting the excretion of the conjugated bilirubin, thus elevating the direct fraction. Exchange transfusion was performed in a full term with a bilirubin level of 25 percent during the first twenty four hours. Fifteen infants had positive blood cultures. Among the organism identified we had ten with hemolytic staph. aureus coagulase positive, two cases with *E. coli*, two with *Pseudomonas* and one with *Klebsiella*.

There are various mechanisms to account for the presence of jaundice, in infants with sepsis. Evidence of hemolysis encountered with a rise in reticulocyte count above 8 percent and polychromasia in peripheral blood smear indicating red cell destruction. Under normal conditions in the newborn there is a daily degradation of 0.5 gm. of hemoglobin yielding 17 mg of bilirubin which is the physiological load of newborn liver. Any portion of this bilirubin which is not metabolized by the liver would remain in the unconjugated form in the serum. Increased formation of bilirubin due to hemolytic process increases the handling load of the liver. The liver capacity to conjugate bilirubin is further enhanced by hepatotoxic factors leading to impairment in the conjugating processes.

There may be competition for albumin-binding sites if such drugs as gantrisin are used. It has been found that chloromycetin competes with bilirubin in the conjugation with glucuronic acid. (5) The use of novobiocin in cases with sepsis may lead to hyperbilirubinemia.

It should be mentioned that the glucuronidating capacity increases with age, that is, the older the infant, the more mature the glucuronyl transferase system (4).

Cyanosis accounts for hyperbilirubinemia in six of the infants investigated.

All of the infants who developed severe cyanosis during the first twenty four hours and associated jaundice were full terms. In five of them jaundice appeared during the third day. Two babies had an increase in bilirubin level above 20 percent at the onset of jaundice. Levels of direct bilirubin above 0.5 mg percent were encountered in three babies. No exchange transfusion was performed. No death was registered.

TABLE III: CYANOSIS (6)

1. All F. T. Cyanosis 1st 24 Hrs.
2. Onset of jaundice - 5 cases - 2nd - 3rd day
3. Total Bil. above 20 mg percent - 2 (F. T.)
4. Direct Bil above 0.50 percent - 3 (FT)
5. Exchange T. O
6. Mortality - 0
7. Mech. prod. jaundice:
 - a. depletion of CHO
 - b. hypoxia-decreases monoglucuronide
 - c. hepatocellular damage - diminishes excretion of conjugated bil.

The mechanism considered in the production of jaundice in these infants with cyanosis were related to various contributing factors. In these infants the delay feeding which leads to depletion of CHO sources. The existing hypoxia contributed to a decrease in the formation of monoglucuronide synthesis extra-hepatically. Hypoxia also leads to hepatocellular damage thus depressing further more a marginally functioning liver.

Cephalohematoma developed in six infants with concomitant jaundice. Of these five were full term and one was premature.

TABLE IV: CEPHALOHEMATOMA (6)

1. 5 Ft. 1 Prem.
2. Onset of jaundice - 2nd. day
3. Total bil. above 20 mg percent-2 (1 Ft and 1 Prem)
4. Direct Bil. above 0.5 mg percent - 5(4 Ft. - 1 Prem)
5. Exchange T. - 0
6. Mortality - 0
7. Mech. prod. jaundice:
 - a. Increased hemolysis with increased formation of bilirubin.

In all instances the onset of jaundice was during the second day of life. Two babies had bilirubin levels above 20 mg percent. One was a full term and other a premature who had a total bilirubin level of 25 percent mg. In five infants (4 Ft and 1 Prem) the direct bilirubin level was above 0.5 mg percent. No exchange was required. There was no death. Jaundice associated with cephalohematoma can be explained in the babies with an increased formation of bilirubin subsequent to increased bleeding in a localized area with increased hemoglobin destruction.

Table V presents a total of six miscellaneous cases with hyperbilirubinemia.

TABLE V: MISCELLANEOUS (6) F.T.

3. (luectic mothers) 1 with bil. above 20 mg. percent		
All 3 with direct bil. above 0.5 mg percent		
Mech. hepatocellular damage.		
1. (diabetic mother-cesarean section) Total bil. above 20 mg percent		
direct bil. above 0.5 mg percent		
Mech. (hypoglycemia)		
1. Inspissated bile syndrome		
D. bil. above 0.5 mg percent	Onset of jaundice-2nd-3rd.	
Mech. obstructive.	day	
	Exchange O	
1. Petechiae of scalp	Death O	
Mech. hypoxia		

In the six miscellaneous cases all of them full term three from luectic mothers who had an elevation in the direct bilirubin fraction indicative of hepatocellular damage. One was delivered by cesarean section from a diabetic mother. The other two had inspissated bile syndrome and petechiae of the scalp respectively.

Summary and Conclusions

In this study investigating the causes of neonatal jaundice we had 76 cases of jaundice not due to hemolytic disease of the newborn. Of these, 35 cases had respiratory distress (21 full term-14 pre-matures) 23 were due to sepsis (14 full term- 9 pre-matures); 6 cases (all full term) were associated with cyanosis during first 24 hours; 6 cases (5 full term, 1 premature) developed cephalohematoma with jaundice and the other 6- all full term were miscellaneous cases: Three from luectic mothers, diabetic mother, one had inspissated bile syndrome, and the other had petechiae of the scalp.

In the majority of cases the onset of jaundice was during the 2nd. and 3rd. day of life. The mechanism for the production of hyperbilirubinemia in the group vary accordingly to the different predisposing factors involved.

In respiratory distress there is the metabolic factor of hypoglycemia. With reduced stores of carbohydrate there is a decrease in the oxidative process of glucose to glucuronic acid which in combination with uridyldiphosphate (the donor) conjugates bilirubin in the presence of glucuronyl transferase (enzyme) in the liver microsome to form the final soluble excretable compound of bilimbin diglucuronide.

Associated with respiratory distress there is respiratory acidosis. At a lower Ph the albumin binding capacity of plasma with bilirubin is altered, thus increasing the level of free insoluble toxic bilirubin in blood serum with subsequent mobilization to tissues.

Another factor involved is the present hypoxia. This leads to hepatocellular damage with depression of the conjugating mechanism of bilirubin.

With sepsis there are two predominant mechanism leading to the production of jaundice. One is the hemolytic process with increased formation of bilirubin thus increasing the handling load of the neonatal liver. The newborn liver is required to clear out 17 mg. of bilirubin per day, since he destroys an average 0.5 gm. of hemoglobin per day under physiologic conditions. The other involved with sepsis is the hepatotoxic factor.

This is a predominant one in *E. Coli* septicemia. With hepatocellular damage there is an increase in the level of direct bilirubin because there is impairment of the cellular process excreting this pigment.

Cyanosis in the newborn leading to hypoxia predisposes to jaundice because of the hepatocellular damage thus decreasing the excretory capacity of the liver. There is an additional factor of the depletion of carbohydrate stores with subsequent depression of conjugation of bilirubin. It has been found that with hypoxia there is a diminished formation of monoglucuronide extra-hepatically. This pigment is finally detoxified within the liver to the diglucuronide form. With hypoxia there is an altered permeability of blood brain barrier and an increase cell susceptibility to toxic effects of bilirubin.

Cephalohematoma predisposes to hyperbilirubinemia because of the increased destruction of hemoglobin with the marked production of bilirubin in a closed space.

The possibility of performing exchange transfusion was contemplated in these cases where the level of indirect bilirubin was above 20 mg. percent during the first six days of life. However each case was individualized and other factors were considered. Maximum levels of bilirubin up to 25-30 mg. percent were attained before final decision for exchange transfusion was reached. The criteria used in evaluation for exchange transfusion in hyperbilirubinemia of non hemolytic origin includes:

1) Neurologic signs of kernicterus as drowsiness, poor sucking, poor more reflex, etc.

2) Sex and size of Infants:

In males there is frequently found a depression of the enzyme activity of glucose 6 PO₄ dehydrogenase,

which is sex linked genetically determined. Incidence of kernicterus is more frequent in premature because of liver immaturity with a deficiency in glucuronyl transferase the enzyme responsible for the conjugation of bilirubin.

3) The presence of large hematomas or echymosis coexistent with an elevated serum bilirubin. These lesions represent a large extravascular mass of hemoglobin which will be metabolized to bilirubin at an accelerated rate.

4) Hydration of the Infant:

If the infant has not been given or has been unable to tolerate adequate fluid intake to meet his metabolic expenditure, the degree of hyperbilirubinemia may represent an artificial elevation due to hypovolemia. Adequate hydration in such instances may be all that is necessary. This appears to be particularly true for the off spring of diabetic mothers.

5) Serum Protein concentration:

If the infant's serum protein concentration is below 5 gm percent an exchange transfusion may be indicated in the case of associated bilirubin 20 mg percent. Additional bilirubin formation may not be reflected in rise in the serum bilirubin concentration, in the presence of marked hypoproteinemia.

6) Evidence of systemic infection:

The infant suffering from sepsis is more predisposed to hyperbilirubinemia. The bilirubin may increase to toxic levels where exchanged transfusion is indicated to prevent complication of kernicterus.

Taking in consideration all the various factors that have been discussed we may conclude that in the case of hyperbilirubinemia of non hemolytic origin there is more elasticity as to the final decision of when to perform the exchange transfusion. Maximum levels of bilirubin up to 25-30 mg percent during first six days of life could be attained before exchange transfusion was contemplated.

Nowadays in our hospital the use of early and continuous phototherapy in the case with hyperbilirubinemia mainly of non hemolytic origin has replaced greatly the need for an exchange transfusion.

Resumen y Conclusiones

En el presente estudio se investigaron las causas de ictericias en 76 recién nacidos que no sufrían de enfermedad hemolítica debido a la incompatibilidad ABO, sub-grupos o Rh o de deficiencias de factores enzimáticos. De estos pacientes, 35 tuvieron "Distress respiratorio". (21 a término y 14 prematuros) 23 sufrieron sepsis (14 a término y 9 prematuros) 6 a término tuvieron ictericia asociada con cianosis durante sus primeras 24 horas, otros 6 casos (5 a término y 1 prematuro) desarrollaron cefalohematoma con ictericia y los restantes 6 bebés a término tenían causas misceláneas; 3 de mamás luéticas, 1 de mamá diabética, 2 con síndrome de bilis espesa y el último tuvo petequias en el cuero cabelludo.

En la mayoría de los casos la ictericia se desarrolló durante las 48 a 72 horas de vida. El mecanismo de producir hiperbilirubinemia varió de acuerdo con los distintos factores contribuyentes.

En el "Distress respiratorio" está el factor metabólico de hipoglicemia con la reducción en las reservas de carbohidrato hay una disminución en el proceso oxidativo de glucosa al ácido glucurónico.

En la célula hepática Uridil-difosfoácido glucurónico en presencia de glucuronil transferasa conjuga la bilirubina a la glucurónica.

Asociado en el "distress respiratorio" tenemos la acidosis respiratoria, alterando la capacidad de la albúmina a transportar la bilirubina libre para mobilizarse al tejido. También la hipoxia existente afecta la célula hepática alterando sus funciones para el metabolismo final de la bilirubina.

Asociado con sepsis tenemos el factor hemolítico produciendo más bilirubina y el factor hepato tóxico alterando el mecanismo de glucuronidación. El hígado del recién nacido metaboliza diariamente los 17 mg de bilirubina producidos de 0.5 gm de hemoglobina al destruirse parcialmente las células rojas.

El factor hepato tóxico producido en sepsis por E. Coli altera los procesos celulares para eliminar la bilirubina diglucurónica— aumentando así la fracción directa en el suero sanguíneo.

Cianosis en el recién nacido dando origen a hipoxia predispone el desarrollo de ictericia al haber daño hepato celular que altera el mecanismo de glucuronidación. Durante un estado de hipoxia se altera la permeabilidad de los capilares y la barrera-sangre-cerebro se rompe haciendo más susceptible la célula cerebral a los efectos tóxicos de la bilirubina.

La necesidad de practicarse una exanguino transfu-

		<u>Ft.</u>	<u>Prem.</u>
Respiratory Distress	35	21	14
Sepsis	23	14	9
Cephalohematoma	6	5	1
Cyanosis	6	6	0
Miscellaneous	6	6	0
Total	76	52	24

sión fue considerada en los casos donde el nivel de bilirubina indirecta alcanzó niveles sobre 20 mg por ciento durante los primeros seis días de vida, sin embargo cada caso fue cuidadosamente evaluado y otros factores fueron tomados en consideración.

Niveles máximos entre 25 a 30 mg por ciento fueron alcanzados antes de tomar la decisión de hacerse una exsanguino transfusión; para evitar el desarrollo de kernicterus y los infantes fueron vigilados estrechamente para el desarrollo de signos neurológicos como apatía, pobre reflejo de succión o del moro, etc. Se consideró la edad y sexo del infante. Es sabido que en los varones es más frecuente encontrar una deficiencia de la actividad enzimática de Glucosa-6 Fosfato de hidrogenasa que está determinada genéticamente.

La incidencia de Kernicterus es más alta en los prematuros con niveles más bajos que en los nenes a término debido a insuficiencia hepática por deficiencia de glucuronil transferasa.

La presencia de grandes hematomas o equimosis representa una mayor producción de bilirubina a un ritmo acelerado dependiendo del grado de hemólisis.

Además de los factores ya mencionados se tomó en consideración la hidratación del paciente. Con hipovolemia debido a deshidratación puede elevarse artificialmente la bilirubina, y con una hidratación adecuada puede beneficiarse el paciente como se pudo ver en los nenes de mamás diabéticas.

Otro factor estudiado al decidirse si era necesario o no una exanguino transfusión fue el nivel de proteína plasmática. Si era menor de 5.5 gm., la formación de nueva bilirubina podía no verse reflejado un aumento correspondiente en el suero, ya que había menos cantidad de albúmina para unirse a bilirubina y por consiguiente esta se fijaba en los tejidos.

Otro punto considerado era la existencia de sepsis con marcada hiperbilirubinemia donde la exanguino transfusión está indicada para prevenir kernicterus.

En conclusión podemos considerar que de acuerdo con los distintos factores discutidos en el tratamiento de la hiperbilirubinemia no producida por enfermedad

hemolítica de incompatibilidad ABO, sub grupo o factores Rh hay más elasticidad en cuanto a los niveles de bilirubina para decidir una exsanguino transfusión. Hoy en día el uso temprano de Fototerapia continúa ha reemplazado en gran parte este procedimiento.

Acknowledgment

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ACTUALIDADES MEDICAS

ABSTRACTOS DE LA CONVENCION ANUAL DE LA ASOCIACION PUERTORRIQUEÑA DEL CORAZON SEPTIEMBRE 29, 30 Y OCTUBRE 1^{RO} 1972 HOTEL CARIBE HILTON SAN JUAN, PUERTO RICO

FIEBRE REUMATICA EN LA EDAD PEDIATRICA EN EL HOSPITAL UNIVERSITARIO

Dra. Mercedes Vega Vidal — Dr. Jorge Sánchez

Se evalúan 124 pacientes con fiebre reumática, 68 varones y 56 niñas entre las edades de cuatro a doce años siendo la edad media de ocho años en el primer ataque; de los cuales 101 casos se diagnosticaron en el hospital y 23 afuera. Once pacientes se readmitieron con recurrencias. En 58 había un historial de faringitis y en ocho historial familiar de fiebre reumática (68).

En admisión, ocho presentaron corea, 25 poliartritis, 19 carditis, 14 de las cuales con fallo cardíaco y 68 presentaron la combinación de corea, carditis y/o artritis. Sólo hubo seis episodios de pericarditis y dos pacientes con nódulos. En cuatro casos había dolor abdominal asociado pero sólo uno con el cuadro de abdomen agudo (54).

El laboratorio reflejó una elevación en la eritrosedimentación en 70 por ciento de las admisiones, el título de antiestreptolisina 0 en 56 por ciento y la proteína C reactiva en 38 por ciento. Sólo 17 por ciento presentaron hemoglobina menor de 10 gramos por ciento y 72 por ciento leucitosis. Cultivos de garganta para *Streptococo* Grupo A,B Hemolítico fue positivo en seis casos y en 13 para *Estafilococo Aureus* (62).

En 55 episodios el electrocardiograma era normal, 30 de éstos debido a prolongación del intervalo P-R. La radiografía del tórax era normal en 42 (25).

En la actualidad, 74 pacientes tienen un corazón normal, 45 tienen daño residual valvular, en cinco no hay información y hubo dos muertes (23).

AORTIC VASCULAR RINGS

Rafael Brito, MD, Enrique Marquez, MD and Efraín Defendini, MD

Although the problem of dysphagia lusoria due to vascular structures has been known since Bayford (1794), who described a case of retroesophageal right subclavian artery; corresponded to Gross in 1945 to report the first surgical success. These so called vascular rings can also compress the trachea adding dyspnea and stridor to the clinical picture. Most of the time the true nature of such symptomatology can be demonstrated the esophagogram or the aortogram. The rings can be formed by combination of structures, the types found more often are: double aortic arch, right aortic arch with ligamentum arteriosus and retroesophageal right subclavian artery arising as the fourth aortic branch.

The present report covers a period from 1962 to 1971, when the first and the last cases of vascular ring were recorded at the University Hospital, Puerto Rico School of Medicine.

Eleven cases, seven males and four females were treated during this period. All of them were younger than one year of age, prior to surgery esophagogram and aortogram were the preferred diagnostic methods. No mortality occurred and all the cases were discharged from the hospital, however there were several complications such as wound infection, atelectasis, gastroenteritis and chylothorax.

It is recommended that in any child showing dysphagia or stridor the diagnosis of vascular ring be suspected and proper diagnostic steps taken mainly the esophagogram. If the diagnosis is confirmed, then surgery is indicated on an urgent basis.

POSTOPERATIVE COMPLICATIONS OF THE MUSTARD PROCEDURE

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The long term prognosis after surgical repair of complete transposition of the great arteries by the Mustard procedure is not yet established. Some of the more frequent late postoperative complications that have been reported include persistent post-operative cardiac arrhythmias, tricuspid insufficiency, pulmonary and/or systemic venous obstruction and intra-atrial baffle defects.

Eleven children repaired with the Mustard procedure between 1965 and 1971 were studied by atrial pacing and cardiac catheterization. Nine had persistent postoperative ectopic cardiac rhythms. Atrial pacing in five suggested sinus node damage in four and A-V junctional conduction tissue damage in one. Superior vena cava angiograms showed leaks through the baffle at the superior vena cava-atrial junction in seven children, that have not previously been demonstrated angiographically. The superior vena cava in one patient was totally obstructed at the superior vena cava-atrial junction. None showed any hemodynamic signs of pulmonary venous obstruction or tricuspid insufficiency.

Apart from one patient with A-V junctional conduction tissue damage, the other three complications in our series seemed to be related to suturing of the intra-atrial baffle in the sinus node region. These findings suggest that improvements in the operative technique of placing the baffle in the vulnerable sinus node region may reduce the incidence of late postoperative complications.

CORRECCION TOTAL DE PACIENTES CON DEFECTO IN- TERVENTRICULAR Y CONSTRICCION QUIRURGICA DE LA ARTERIA PULMONAR

Edda Torres de Arraut, MD – Felipe Vizcarrondo, MD

En este trabajo se analiza la data clínica de 30 pacientes, con una edad media de 7.7 años operados en el Hospital Universitario desde agosto 1967 a marzo 1972. Todos estaban en fallo cardíaco intractable al operarse paliativamente; en el 70 por ciento de los casos esto fue antes del primer año de edad. El tiempo entre la paliación y la operación correctiva varió de 4 a 11 años.

Todos los pacientes fueron cateterizados antes de la corrección total. El 97 por ciento de los pacientes demostró hipertensión ventricular derecha. La presión pulmonar fue menor de 30 mm Hg excepto en 3 casos. En 90 por ciento de los pacientes se demostró cortocircuito de izquierda a derecha. En 43 por ciento se demostró además cortocircuito de derecha a izquierda. En dos pacientes se encontró el defecto interventricular espontáneamente cerrado.

Todos los defectos interventriculares se corrigieron a través de ventriculotomía derecha, en 50 por ciento con un parche y en el resto por sutura directa. En 37 por ciento se utilizó un parche de pericardio para ensanchar el área de constricción en la arteria pulmonar y en dos se hizo infundibulectomía.

La re-evaluación post-operatoria de los pacientes ha demostrado que todos, excepto uno, están asintomáticos. Todos tienen soplo eyectivo en el área pulmonar, seis tienen soplo de defecto interventricular residual y tres, soplo de insuficiencia pulmonar. Un paciente tiene soplo de defecto interventricular, estenosis e insuficiencia pulmonar asociados con cardiomegalia y poca tolerancia al ejercicio.

Se correlacionan los hallazgos clínicos, electrocardiográficos y radiológicos antes y después de la operación, y se discuten las complicaciones y mortalidad del procedimiento.

TRASTORNOS DE LA CONDUCCION DESPUES DE LA CORRECCION COMPLETA DE LA TETRALOGIA DE FALLOT

Felipe Vizcarrondo, MD – Joaquín Mendoza, MD

Los bloqueos fasciculares después de la reparación de la Tetralogía tienen complicaciones clínicas reconocidas, sin embargo, el pronóstico a largo plazo no está definido aún. Este trabajo analiza nuestra experiencia con 15 pacientes pediátricos y hace hincapié en las serias situaciones clínicas producidas a consecuencia de estos trastornos.

El diagnóstico en todos los pacientes se hizo por cateterismo y angiocardiógrafía y se confirmó por la cirugía. En la mayoría se cerró el defecto interventricular con un parche a través de una ventriculotomía y se hizo miomectomía infundibular. Varios tuvieron parche del infundíbulo y algunos del infundíbulo y la arteria pulmonar.

Los electrocardiogramas pre-operatorios mostraron eje a la derecha, PR normal y ancho de QRS normal. Los post-operatorios mostraron bloqueo de rama derecha (BRD), hemibloqueo izquierdo anterior (HIA) y bloqueo trifascicular.

Dos de nuestros pacientes requirieron implantación de marcapaso al desarrollar episodios de síncope después de la cirugía.

Estos trastornos de conducción se pueden clasificar en varios grupos:

1. BRD sin complicaciones clínicas inmediatas y a los 5 años de seguimiento.

2. BRD y HIA sin complicaciones clínicas.
3. BRD y HIA con HIP intermitente con serias implicaciones clínicas.
4. BRD y HIP.
5. BRD y HIP con HIA intermitente.
6. Bloqueo atrioventricular completo.

Esta presentación discute los trastornos de conducción y las complicaciones que presentaron nuestros pacientes y señala la importancia de reconocerlos a tiempo para así evitar consecuencias que puedan causarle la muerte.

LA VALVULA TRICUSPIDEA: NUEVAS ALTERNATIVAS.

Jorge O. Just Viera, MD – Olga Rodríguez, MD

Trabajos recientes reflejan una actitud quirúrgica más agresiva para el tratamiento de atresia valvular tricuspídea, hipoplasia ventricular derecha y endocarditis de la válvula tricuspídea. Estas nuevas alternativas merecen ser discutidas por representar soluciones diferentes a problemas, que aunque infrecuentes, son sumamente complicados.

ATRESIA AORTICA EN EL RECIEN NACIDO

Jorge Sánchez, MD, Georgina Marroig, MD, Ofelia Rojas, MD, A. Martínez Picó, MD

La incidencia de cardiopatías en el neonato es alrededor del 1 por ciento, la mortalidad del 30 por ciento, ocupando la atresia aórtica el primer lugar. De los 14 casos de autopsia 9 fueron hembras, y 5 varones, el peso promedio fue 5.7 lbs. y la edad de muerte 7 días (2 a 30). Todos presentaron fallo cardíaco y segundo sonido sencillo, 13 shock, 12 cianosis, 10 soplo, 9 pulsos débiles, 3 normales y dos ausentes. Lo más importante fue un precordio activo con pulsos débiles. Había cardiomegalia considerable (> 55 por ciento) con congestión pulmonar en todos a la radiografía. El electrocardiograma mostró eje derecho en 12, izquierdo en 2, hipertrofia ventricular derecha en todos, de atrio derecho en ocho. Al cateterismo habían presiones sistémicas en ventrículo derecho y pulmonar, hipertensión de atrio izquierdo con gradiente entre ambos atrios, cortocircuito de izquierda a derecha en atrio y derecha a izquierda en aorta.

Trece pacientes tuvieron al angiograma: Atresia aórtica y mitral, hipoplasia ventricular izquierda, aorta ascendente y conducto arterioso adecuado. La autopsia reveló en todos corazón derecho grande con conducto arterioso adecuado, atresia aórtica, hipoplasia de ventrículo izquierdo, aorta ascendente y transversa, con atresia mitral en 13 y estenosis en uno. Tres tuvieron defecto interatrial, 10 foramen oval pequeño, 1 grande y 1 foramen oval y defecto interatrial. El tamaño de la comunicación interatrial tenía relación directa con la edad de la muerte. Tres tuvieron defecto interventricular.

Como el tratamiento de estos pacientes es inefectivo es necesario diferenciarlos de los con cardiopatías corregibles.

HALLAZGOS FONOCARDIOGRAFICOS EN LA ATRESIA TRICUSPIDEA

Rafael Villavicencio, MD – Jorge Sánchez, MD

Existen estudios clínicos hemodinámicos y patológicos de esta anomalía, pero no fonocardiográficos. Este trabajo describe los fonocardiogramas en 15 pacientes cuyo diagnóstico de atresia tricuspídea fue comprobado por cateterismo o cirugía. De estos 15, 10 son mujeres y 5 varones cuyas edades fluctúan entre 7 meses y 8 años con una edad media de 2 años. Todos eran cianóticos y están operados paliativamente (10 Potts, 3 Glenn y 2 Blalock-Taussig) y 13 padecieron episodios anóxicos antes de la cirugía.

Las radiografías de tórax demostraron hipertrofia ventricular izquierda con vascularidad normal o aumentada y el electrocardiograma hipertrofia ventricular izquierda en 15 y de atrio derecho en 13.

Los fonocardiogramas mostraron el primer sonido de intensidad normal en todos. Sólo uno presentó un segundo componente en el apex y foco tricuspídeo, el resto tuvieron sólo un componente. La duración total varió de 0.03 a 0.049 seg. y en ningún caso fue más del 19 por ciento de la duración de sístole.

El segundo sonido fue normal en intensidad y sencillo en todos por ausencia del componente pulmonar. Quince presentaban soplo holosistólico, cinco ejetivo y uno continuo.

En el estudio se comenta el significado de un primer sonido angosto y sencillo y el rol de la válvula tricúspide en la producción del primer sonido, también se hace notar el hecho de no registrarse el cierre de la válvula pulmonar aún en casos de hallarse esta válvula anatómicamente presente.

STUDIES OF THE HEMODYNAMIC FACTORS INVOLVED IN RENAL HYPERTENSION

José L. Cangiano, MD, O. Ramírez Muxó, MD, R. Ramírez González, MD and A. Trevino, MD. Veterans Administration Hospital

Studies were undertaken in 10 normal subjects, 10 essential hypertensive and 23 uremic patients to assess their cardiac hemodynamic patterns. Cardiac output, intraarterial blood pressure and peripheral vascular resistance index were measured. Mean cardiac index in 23 uremic patients (4.38 L/min/m^2) was higher ($p < 0.01$) than that of 10 normal volunteers (3.63 L/min/m^2) and 10 essential hypertensives (3.35 L/min/m^2). Stroke index was not significantly different in normal (48.0 ml/beat/m^2), essential hypertensive (47.3 ml/beat/m^2) and uremics (52.1 ml/beat/m^2). The mean peripheral vascular resistance index (PVRI) of uremic patients ($2067 \text{ dynes-sec-m}^2/\text{cm}^5$) was not different than that of normal subjects ($1961 \text{ dynes-sec-m}^2/\text{cm}^5$). However, mean PVRI of hypertensive uremics ($2466 \text{ dynes-sec-m}^2/\text{cm}^5$) was higher than normotensive uremics ($1798 \text{ dynes-sec-m}^2/\text{cm}^5$) with no difference in cardiac index, heart rate or stroke index. These studies show that hypertension in uremia is only sustained by an increase in total peripheral vascular resistance. Increased cardiac output does not appear to be related to hypertension in uremia.

UN PROGRAMA PARA LA DETECCION Y EL TRATAMIENTO EN MASA DE LA HIPERTENSION

Elí A. Ramírez, MD, FACP

La hipertensión arterial es segunda solamente a la enfermedad arterioesclerótica coronaria como causa de muerte e incapacidad entre los hombres de nuestro país. El estudio nacional de salud ha demostrado que de un 15 a un 20 por ciento de los adultos tienen hipertensión según el criterio de una presión casual sobre 160 mm. Hg. sistólica y/o una diastólica de 95 mm. Hg. o más. Estos estudios han demostrado que una alta proporción de estos pacientes no saben que tienen hipertensión, no se están tratando, o están tratando inadecuadamente.

Recientemente el grupo de estudio sobre la hipertensión de la Administración de Veteranos ha presentado evidencia conclusiva de que el tratamiento con drogas antihipertensivas es efectivo en reducir o eliminar las principales complicaciones de la hipertensión.

Como puede esta nueva información ser aplicada para el beneficio de los muchos millones de personas con hipertensión que no están recibiendo esta protección al presente? Claramente se necesita una cuidadosa planificación a largo plazo para poder atacar con éxito un problema de tan gran magnitud. Se presentará una proposición para el establecimiento de estudios piloto, de los cuales se pueden derivar programas para la detección, evaluación y control de la hipertensión en la población veterana y posiblemente en todo el país.

SERUM RENIN AS A DETERMINANT OF TREATMENT IN HYPERTENSIVE DISORDERS

José Campos, MD, José Cangiano, MD, E. Waddell, BS, R. Ramírez González, MD and O. Ramírez Muxó, MD

The role of the renin-angiotensin system has been thoroughly investigated in various hypertensive disorders. Renal hypertension can be associated with hyperreninemia for which corrective surgery has been successful. Adrenal hypertension, adenoma or hyperplasia can be associated with hyporenemic states for which surgery and/or specific medical therapy is recommendable. Our presentation will cover our present experience at the Veterans Administration Hospital with both hyper and hyporeninemic states. Clinical cases of hyperreninemia associated with both end stage renal disease and renal artery stenosis, and hyporeninemia associated with both excessive aldosterone levels and a normoaldosterone state will be described. The results of both surgical and medical therapy will be presented.

LA GAMAGRAFIA PULMONAR EN LAS CARDIOPATIAS CONGENITAS

Aldo E. Lanaro, MD, René Dietrich, MD, Agustín Muñoz, MD, Amalia Martínez Picó, MD

Las malformaciones congénitas del corazón presentan alteraciones en el flujo pulmonar, cuya determinación es de importancia en el diagnóstico y tratamiento de los pacientes.

En la actualidad la gamagrafía es el método más sencillo, traumático y exacto para la determinación de la distribución del flujo sanguíneo pulmonar, que no siempre se aprecia en una radiografía corriente de tórax, y además no requiere hospitalización del paciente.

Se realizaron 43 pruebas en 36 pacientes con cardiopatías

congénitas cuyas edades variaron entre 15 días y 12 años. Se estudiaron en el gamágrafo rectilinear y la Cámara de Centelleo utilizando Macroagregados marcados con ^{131}I odo o $^{99\text{m}}\text{Tc}$ ecnecio.

Resultados:

1. DISTRIBUCION IGUAL DE LA RADIATIVIDAD EN AMBOS PULMONES: que significa (1) Normalidad en la perfusión pulmonar: 7 casos. (b) Perfusión pulmonar por vía de las bronquiales: 4 casos.

2. INVERSION DE LA RELACION DE RADIATIVIDAD

APICE/BASE - que indica aumento del flujo pulmonar o hipertensión pulmonar: 2 casos.

3. DISMINUCION TOTAL O SEGMENTAL DE LA RADIATIVIDAD EN UN PULMON - que refleja: (a) Alteración de la perfusión en dicha área: 14 casos (4 en pulmón derecho y 10 en pulmón izquierdo). (b) Irrigación del pulmón por un cortocircuito quirúrgico: 16 casos.

Los estudios han sido realizados en el Centro Nuclear de Puerto Rico cuyas facilidades se encuentran disponibles para los pacientes que las necesiten.

NOTICIAS

From Larry R. Pilot, Director, Division of Compliance, Office of Medical Devices, Department of Health, Education, and Welfare, Food and Drug Administration, Rockville, Maryland.

We are writing to inform you of recent Court actions involving the Diapulse Pulsed High Frequency Generator devices, manufactured and distributed by the Diapulse Corporation of America. The injunction restrains the firm from shipping, selling or offering Diapulse devices for sale in interstate commerce.

On June 9, 1972, the District Court granted a Permanent Injunction prohibiting the interstate shipment of the device. The Court held the Diapulse to be misbranded by false and misleading labeling claims representing that the device is effective for the treatment of a wide variety of disease conditions.

Over 4,000 of these devices have been marketed, primarily to hospitals, clinics, medical and osteopathic physicians, chiropractors and other practitioners, some of whom may be members of your association. All units manufactured to date are considered in violation of the law and subject to seizure. We are now initiating action against the Diapulse devices shipped in interstate commerce.

We are taking this opportunity, in the interest of mutual cooperation, to seek your assistance in removing these ineffective and violative products from use. We request that you convey the contents of this letter to all members of your association.

We will be glad to assist anyone who may wish voluntarily to dispose of his device(s) and avoid the embarrassment of a seizure action which becomes a matter of public information. Anyone wishing to offer voluntarily to destroy his device, otherwise render it inoperable or surrender the device to FDA may do so by contacting any of our offices.

Announcement of Postgraduate Course:

CLINICAL GASTROENTEROLOGY — September 10-16, 1972; Castle Harbour Hotel, Bermuda. Vernon M. Smith, M. D., Director, 301 St. Paul Place, Baltimore, Md., 21202.

Del American College of Physicians:

La reunión anual regional del capítulo de Puerto Rico del American College of Physicians se celebrará la noche del viernes 13 de octubre y la mañana del sábado 14 de octubre de 1972 en asociación con la sección de Medicina Interna de la Asociación Médica de Puerto Rico. La sesión científica del viernes por la noche se llevará a efecto en el auditorio de la Asociación Médica de Puerto Rico. La sesión del sábado por la mañana se celebrará en el anfiteatro de la Escuela de Medicina en el

Centro Médico de Puerto Rico.

El huésped de honor será el Dr. Julius E. Stolfi, FACP, Vice Presidente, American College of Physicians, quien será el representante oficial del Colegio. El programa científico es sumamente atractivo e incluye varias ponencias libres y discusiones de paneles. El programa completo se publicará próximamente.

Se extiende una cordial invitación a los miembros del Colegio en Puerto Rico, a los miembros de la Asociación Médica de Puerto Rico, a los residentes e internos de los centros médicos de Puerto Rico y sus instituciones afiliadas, y a los estudiantes de la escuela de medicina de la Universidad de Puerto Rico. Elí A. Ramírez Rodríguez, MD, FACP, Gobernador para Puerto Rico.

Jury Says Life Ends When Brain Stops

When does death occur? A Richmond, Va. jury in a recent heart transplant suit linked the time of death with the death of the brain—even if other organs continue to function. Dr. Dr. David M. Hume, chief of surgery at the Medical College of Virginia Hospital, and three other defendants were exonerated in the death of a heart donor, in a \$100,000 damage suit filed by the donor's brother.

The brother charged that the donor was still alive when the heart was removed since the heart and respiratory systems were still functioning. His attorney, State Sen. L. Douglas Wilder, further accused the transplant team of speeding the donor's death by shutting off the mechanical support system.

Medical witnesses countered that while the vital signs were kept going by the machines to keep the heart and kidneys intact for transplant purposes, Bruce O. Tucker, the donor, was "neurologically dead" because his brain showed no activity for several hours before the operation.

Virginia law defines death as the total cessation of all body functions. The case will be appealed to the Virginia Supreme Court.

Mediation Panels Settle Medical Malpractice Suits

A new experimental program set up in New York City to settle medical malpractice suits appears to be working.

The program involves three-man mediation panels composed of a judge, a lawyer and a physician. Since its inception in September 1971, one third of the cases presented have been resolved without going to trial.

The program was instituted after the formation of a Joint Interprofession Committee of Doctors and Lawyers in New York last fall, headed by former ATL President Jacob Fuchsberg and Dr. Carl Goldmark Jr.

According to reports, cases involving municipal hospitals

and physicians employed by the city have offered the most difficulties to mediation because of a lack of a clearly defined line of authority and the intricacies of a large bureaucratic structure.

American College of Surgeons Postgraduate Courses 1972-73:

- Course No. 1 — Basic Mechanisms in Internal Medicine - September 25-29, 1972, Medical College of Virginia, Division of Health Sciences, Virginia Commonwealth University, Richmond, Virginia 23219. Meeting Place - Baruch Auditorium, Egyptian Building, Marshall and School Streets, Richmond, Virginia. Director - W. T. Thompson, Jr., MD, FACP - Minimum Number of Registrants, 100; Maximum, 175.
- Course No. 2 — Current Concepts in Hematology, October 2-4, 1972, University of Pittsburgh School of Medicine. Meeting Place - Auditorium, Montefiore Hospital, University of Pittsburgh Health Center, Pittsburgh, Pa. Co-Directors, Marvin Lewis, MD, FACP, Dane Boggs, MD; Associate Director, William Cooper, MD, FACP. Minimum Number of Registrants, 60; Maximum, 180.
- Course No. 5 — Advances in Therapeutics and Clinical Pharmacology - October 9-11, 1972, University of Florida, Gainesville, Fla. Meeting Place - 2nd Fl. Auditorium Reitz Union, University of Florida. Co-Directors: W. Walter Oppelt, MD, L. E. Cluff, MD, FACP. Minimum Number of Registrants, 25; Maximum, 150.
- Course No. 6 — Human Reproduction, Population Problems and Fertility Control - October 9-12, 1972, Harvard Medical School, Boston, Mass. Meeting Place - Seminar Room, 1st fl. Laboratory of Human Reproduction and Reproductive Biology, 45 Shattuck Street, Boston, Mass. 02115. Director: Roy O. Greep, Ph.D. Minimum No. of Registrants, 75; Maximum 200.
- Course No. 7 - Recent Advances in Infectious Diseases, in Honor of Dr. Wesley W. Spink, Regents' Professor of Medicine and Comparative Medicine, Past President ACP. October 12-14, 1972, University of Minnesota Medical School, Minneapolis, Minnesota. Meeting Place - Mayo Memorial Auditorium, Director: Wendell H. Hall, MD, FACP, Co-Director: Robert P. Gruninger, MD. Minimum Number of Registrants, 50; Maximum, 200.
- Course No. 8 - Current and Future Concepts in Gastroenterology, November 6-8, 1972. Meeting Place - Main Auditorium, Arizona Medical Center, College of Medicine, Tucson, Arizona. Co-Directors: David C. H. Sun, MD, FACP, Charles L. Krone, MD, ACP. Member, Arie C. Van Ravenswaay, MD, FACP. Minimum Number of Registrants, 100; Maximum, 250.

A. C. P. Postgraduate Courses 1972-73:

- | No. | Date | Title Location |
|-----|------------------|---|
| 9 | Nov. 8-10, 1972 | Internal Medicine Grand Rounds, Mayo Clinic, Rochester, Minn. |
| 10 | Nov. 15-17, 1972 | In Vitro Procedures in Nuclear Medicine, Johns Hopkins Medical Institutions, Baltimore, MD. |
| 11 | Dec. 4-8, 1972 | Advances in Diagnosis and Treatment in Clinical Medi- |

- | | | |
|----|----------------------|--|
| 12 | Jan. 8-10, 1973 | Three Days of Liver Disease, Emory University School of Medicine, to be held at Disneyland Hotel, Anaheim, Calif. |
| 13 | Feb. 8-10, 1973 | Recent Advances in the Immunoprophylaxis and Chemotherapy of Infectious Diseases, University of Arizona College of Medicine, Tucson, Ariz. |
| 14 | Feb. 26-Mar. 2, 1973 | Clinical Gastroenterology, University of Michigan Medical Center, Ann Arbor, Mich. |
| 15 | Mar. 5-8, 1973 | Problems of International Health, Naval Hospital San Diego, to be held at LeBaron Hotel, San Diego, Calif. |
| 16 | Mar. 5-8, 1973 | Modern Neurological Diagnosis and Therapy, University of Miami, to be held at Eden Roc Hotel, Miami Beach, Fla. |
| 17 | Mar. 12-16, 1973 | Infectious Diseases, University of Maryland School of Medicine, Baltimore, Md. |
| 18 | Mar. 14-16, 1973 | Clinical Pharmacology-Rational Basis of Therapeutics, University of California School of Medicine, San Francisco, Calif. |
| 19 | Mar. 19-23, 1973 | Four and One-Half Days of Internal Medicine: What's New?, University of Alabama Medical Center, Birmingham, Ala. |
| 20 | Mar. 22-24, 1973 | Clinical Recognition and Management of Heart Disease, 1973, Arizona Medical Center Hospital, Tucson, Ariz. |
| 21 | Mar. 26-30, 1973 | Cardiology, 1973. Topics of Current Interest, Mount Sinai School of Medicine, New York; to be held at the Americana, New York. |
| 22 | Apr. 4-6, 1973 | Recent Advances in Diagnosis and Management of Pulmonary Disease, Virginia Mason Medical Center, Seattle, Wash. |
| 23 | Apr. 24-27, 1973 | Pulmonary Disease, University of Pennsylvania School of Medicine, Philadelphia, Pa. |
| 24 | Apr. 25-27, 1973 | Hepatobiliary Disease in Clinical Practice, Co-sponsored by Presbyterian Hospital of Pacific Medical Center and the Department of Gastroenterology, University of California, San Francisco, to be held at the Hilton Hotel in San Francisco, Calif. |
| 25 | Apr. 25-27, 1973 | Advances in Diagnosis and Management of Infectious Disease, University of Wisconsin, Madison, Wis. |
| 26 | May 16-18, 1973 | The Rheumatic Disease - Clinical and Immunological Aspects, University of Texas Southwestern Medical School, Dallas, Tex. |
| 27 | May 16-18, 1973 | Clinical Auscultation of the Heart, Georgetown University, Washington, D. C. |
| 28 | May 21-25, 1973 | Internal Medicine, Current Concepts of Clinical Pro- |

- blems, 1973, University of Cincinnati Medical Center, Cincinnati, Ohio.
29. May 21-25, 1973
Intensive Care Units, St. Vincent's Hospital, New York, N. Y.
30. May 29-June 1, 1973
Recent Advances in Endocrinology and Their Clinical Applications, Royal Victoria Hospital, Montreal, Que., Can.
31. June 4-8, 1973
Hematology, University of Washington School of Medicine, Seattle, Wash.
32. June 11-15, 1973
Oncology and Chemotherapy, University of Southern California, Los Angeles, Calif.
33. June 18-22, 1973
Clinical Aspects of Blood Transfusion, Michigan State University, East Lansing, Mich.
34. June 25-29, 1973
Advances in Internal Medicine: Recent Perspectives, 1973, University of Alberta and University of Calgary, to be held at Banff School of Fine Arts, Banff, Alta., Can.

CURSO DE PERFECCIONAMIENTO — SCHOOL CALENDAR
August 1972 - February 1973

August 1	Registration and Medical Examination
August 2	Orientation: E. Belén Trujillo, Curso Staff and Curso Alumnus
August 3-4	Cellular and Developmental Biology
August 7-9	Cellular and Developmental Biology
August 10-11	Psychiatry
August 14-16	Psychiatry
August 17-18	Community Medicine
August 21-23	Community Medicine
August 24-25	Nutrition
August 28-30	Nutrition
Aug.31-Sept.1	Neurosciences
Sept. 4	HOLIDAY
Sept. 5-8	Neurosciences

Sept. 11-14	Neurosciences
Sept. 15	Endocrinology
Sept. 18-21	Endocrinology
Sept. 22	Kidney, Fluid and Electrolyte Balance
Sept. 25-28	Kidney, Fluid and Electrolyte Balance
Sept. 29	Infections
Oct. 2-6	Infections
Oct. 9	HOLIDAY
Oct. 10-13	Infections
Oct. 16-20	Cardiovascular System
Oct. 23	HOLIDAY
Oct. 24-27	Cardiovascular System
Oct.30-Nov.3	Cardiovascular System
Nov. 6	Cardiovascular System
Nov. 7	HOLIDAY
Nov. 8-10	Respiratory System
Nov. 13-17	Respiratory System
Nov. 20	HOLIDAY
Nov. 21-22	Respiratory System
Nov. 23	HOLIDAY
Nov. 24	Liver and Digestive System
Nov.27-Dec.1	Liver and Digestive System
Dec. 4-7	Liver and Digestive System
Dec. 8	Hematology
Dec. 11-15	Hematology
Dec. 18-19	Hematology
Dec. 20-22	Obstetrics and Gynecology
Dec.25-Jan.5	CHRISTMAS VACATION
Jan. 8-10	Obstetrics and Gynecology
Jan. 11	HOLIDAY
Jan. 12	Obstetrics and Gynecology
Jan. 15-17	Obstetrics and Gynecology
Jan. 18-19	Pediatrics Special Topics
Jan. 22-24	Pediatrics Special Topics
Jan. 25-26	General Surgery and Specialties
Jan.29-Feb. 2	General Surgery and Specialties
Feb. 5	General Surgery and Specialties
Feb. 6-7	Urology
Feb. 8	Rheumatology
Feb. 9	Dermatology
Feb. 10	Final Examination

FE DE ERRATA

Por un error involuntario, se omitió el nombre del Dr. José E. Sifontes, como co-autor del artículo "Post Graduate Medicine in Puerto Rico (A Refresher Course)" además del Dr. Egidio S. Colón Rivera, y publicado en el Volumen 64, Núm. 8, de la edición de agosto de 1972, lo que hacemos constar en esta Fe de Errata.

A N U N C I O S

PHYSICIAN

Fluent in Spanish language, and English, experienced in general or specialized practice, licensed in the State of Illinois, to assist doctor in busy general practice. Excellent compensation - Many fringe benefits - Partnership Potential. Kindly submit all responses to Novak and Schain, Suite 1025, 33 North Dearborn St., Chicago, Illinois 60602.

Edificio en construcción, cuatro apartamentos, oficina o vivienda - Calle Rodrigo de Triana, Hato Rey, cerca Hospital del Maestro. Inf.: Arq. Horacio Díaz, tel. 766-2133.

Who put the C in Mrs. Murphy's orange juice?

Who did encourage high levels of vitamin C in fruit juices? Who fortified milk with vitamin D? Condemned water pollution way back in 1895? Urged creation of the Federal Food and Drug Administration? Recommended seat belts in 1954?

The AMA. Surprising? Not really. Since its inception, the AMA has worked to protect and improve the public health. In a very real sense, it was the forerunner of consumerism.

Today, the AMA is actively involved in virtually every facet of health care. It is engaged in programs to provide more doctors for slum and rural areas. Programs to solve the problems of drug and alcohol abuse, mental health, malnutrition.

In Washington, the AMA has lobbied successfully for more doctors, maternal and child programs, anti-pollution laws, voluntary national health insurance.

It is financing promising pilot programs such as mobile health vans in Chicago's slums, a drug abuse center in Harlem and a Medex program in Washington state.

The AMA does all these things — and more — for the public health. With your support, we can do even more. Find out more about what the AMA does for the public and you. Send for the pamphlet, "The AMA and the American Doctor: Sharing a Common Goal." Write: Dept. DW, at the address below.

**JOIN US.
WE CAN DO MUCH MORE TOGETHER.**

American Medical Association
535 North Dearborn Street/Chicago, Illinois 60610



Call it what you will, it may be premalignant

Before

3/29/67 Before therapy with 5%-FU cream. Patient P. T. shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

After

6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.





Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

and Efudex® (fluorouracil) 5% cream can resolve it.

Call it actinic, solar or senile keratoses,
many regard it as "precancerous."^{1,2}

Topical fluorouracil, considered by some dermatologists to be a major advance in the treatment of multiple solar keratoses,^{3,4} offers the physician a relatively inexpensive alternative to cryosurgery, electrodesiccation and cold knife surgery. Of the topical fluorouracils available, only Efudex offers 2% and 5% solution and 5% cream formulations—formulations that have proved effective in the treatment of these multiple lesions.

Usual duration of therapy, 2 to 4 weeks.

Studies showed that with the 2% and 5% Efudex preparations, the usual duration of therapy was only 2 to 4 weeks.⁵ Other studies with topical fluorouracil revealed that when concentrations of less than 2% were used, significant numbers of lesions recurred.⁶

Treats the lesions you can't see, too.

Numerous lesions, not apparent prior to 2% and 5% Efudex therapy, manifested themselves by definite reactions, while intervening skin remained relatively unaffected.⁵ The early eradication of these subclinical lesions (which may otherwise have undergone further progression) probably accounts for the reduced incidence of future solar keratoses in patients treated with topical fluorouracil—especially with 5% concentrations.⁶

How to identify solar keratoses.

Typically, the lesion—a flat or slightly elevated brown to red-brown papule—is dry, rough, adherent and sharply defined. Multiple lesions are the rule.

Predictable therapeutic response.

The response to a typical course of Efudex therapy is usually characteristic and predictable. After 3 or 4 days of treatment, erythema begins to appear in the area of keratoses. This is followed by a moderate to intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of this response generally occurs two weeks after the start of therapy and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. Lesions that do not respond should be biopsied.

References: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York, Grune & Stratton, 1967, p. 842. 2. Dillaha, C. J.; Jansen, G. T., and Honeycutt, W. M.: "Treatment of Actinic Keratoses with Topical Fluorouracil," in Waisman, M. (ed.): *Pharmaceutical Therapeutics in Dermatology*, Springfield, Ill., Charles C Thomas, 1968, p. 92. 3. Belisario, J. C.: *Cutis*, 6:293, 1970. 4. Sams, W. M.: *Arch. Derm.*, 97:14, 1968. 5. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and Klein, E.: *Cancer*, 25:450, 1970.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

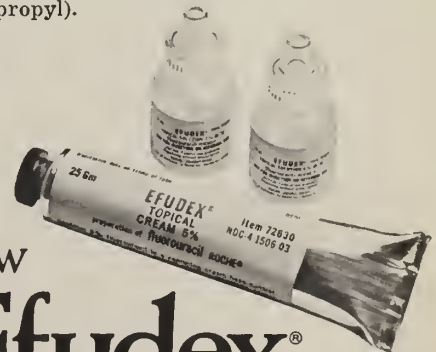
Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



now

Efudex®
(fluorouracil)
cream/solution

*ANOTE AHORA MISMO
EN SU CALENDARIO*

CONVENCION ANUAL AMPR

HOTEL SAN JUAN

NOVIEMBRE 15--18

Cuando comen lo que les gusta
y no lo que deben...



ayude a cubrir "el déficit" de vitaminas con

Unicap Therapeutic

10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
Vitamina D	10 mcg.
Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Ácido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

Upjohn

PR 5226.1 MAY, 1969

6811 MARCA REGISTRADA EN E.U.A.: UNICAP THERAPEUTIC

UPJOHN INTER-AMERICAN CORPORATION / CAPARRA / PUERTO NUEVO

Will his return to work mean the return of undue psychic tension?



When it's mandatory to keep the post-coronary patient calm, consider Valium (diazepam).

Although he's promised to take it easy back on the job, you know he's going back to the same stressful circumstances that may have contributed to his hospitalization. If he experiences excessive anxiety and tension because of overreaction to stress, your prescription for Valium can bring relief. During the period of readjustment Valium can quiet undue anxiety.

For moderate states of psychic tension, 5-mg or 2-mg Valium tablets *b.i.d.* to *q.i.d.* can usually provide reliable relief. For severe tension/anxiety

states, the 10-mg tablets often produce desired results.

The most commonly reported side effects are drowsiness, ataxia and fatigue. Until individual response is determined, caution patient against driving or operating dangerous machinery.

Valium® (diazepam)

For the tense cardiac patient who must be kept calm

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures.

Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision.

Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg *b.i.d.* to *q.i.d.*; alcoholism, 10 mg *t.i.d.* or *q.i.d.* in first 24 hours, then 5 mg *t.i.d.* or *q.i.d.* as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg *t.i.d.* or *q.i.d.*; adjunctively in convulsive disorders, 2 to 10 mg *b.i.d.* to *q.i.d.*. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg *t.i.d.* or *q.i.d.* initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110



BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

PROGRAMA ASAMBLEA ANUAL AMPR	256
RESUMENES DE TRABAJOS PRESENTADOS EN EL PROGRAMA CIENTIFICO	270
TREATMENT OF DRUG RESISTANT HYPERTENSION IN CHRONIC KIDNEY DISEASE 279	
<i>José L. Cangiano, MD, Rafael Ramírez González, MD, Osvaldo Ramírez-Muxó, MD, Enrique Pijem, MD and Elaine Waddell, BS</i>	
EDITORIAL	283
Programa Control de Enfermedades Venéreas: Función y Objetivos	
ACTUALIDADES MEDICAS	284
Criteria and Techniques for the Diagnosis of Gonorrhea Resumen de las Recomendaciones del Comité Asesor sobre Terapéutica - Centro de Control de Enfermedades - Atlanta, Georgia	
NOTICIAS	289





Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Valium® (diazepam)

To help you manage excessive psychic tension



the uncover girl...

Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for

Her contact dermatitis* cleared smoothly by **Vioform®-Hydrocortisone** (iodochlorhydroxyquin and hydrocortisone)

Nothing defeats today's abbreviated clothing styles like an exposed skin disorder. That's why physicians and patients have come to depend on the multiple benefits of Vioform-Hydrocortisone. Because it combines the antibacterial, antifungal actions of Vioform with the anti-inflammatory and antipruritic actions of hydrocortisone, Vioform-Hydrocortisone can prove effective in so many common skin disorders—where topical steroids alone can't cope with frequently coexisting bacterial or fungal infection.

antifungal • antibacterial • anti-inflammatory • antipruritic

*This drug has been evaluated as possibly effective for this indication. See brief prescribing information.



gnosis of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Adverse reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

USAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl

sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. *Lotion*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

2/4711-1 17

C I B A

BOLETIN

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Fundado en 1903

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Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

Second Class postage paid at San Juan, Puerto Rico.



rheumatoid arthritic blowup...

Tandearil® Geigy

oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close observation. Obtain a detailed history, and complete physical and laboratory examination (complete blood count, urinalysis, etc.) before prescribing and at regular intervals thereafter. Carefully select patients, including those responsive to routine measures, contraindicated patients or those who cannot be observed adequately. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of water. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral ulcers (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or loss. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty. **Contraindications:** Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Precautions: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; leukitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy. **Warnings:** Age, weight, dosage, duration of therapy, presence of concomitant diseases, and concurrent use of chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially and periodically to detectable benefits against potential risk of severe, or fatal, reactions. The disease condition itself is

unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonyleurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

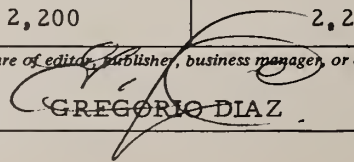
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly check (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal

distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B) 98-146-800-E

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

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**if skin is infected,
or open to infection...
choose the topical
that gives your patient—**

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin[®] Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical aftercare, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

We're not against all her E.coli...

only the E.coli in her
urinary tract



Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis*...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. And it does not suppress normal bac-

**Basic in cystitis*, pyelitis*,
pyelonephritis***

The one-tract action of

Macrochantin® Capsules
(nitrofurantoin macrocrystals) 50mg/100mg

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and a small percentage of ethnic groups of Mediterra-

nean and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms.

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg.

EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04).



Originators and Developers of The Nitrofurans
EATON LABORATORIES
Norwich International
410 Park Avenue, New York, N.Y. 10022

¿Habla español?

If not, the new Rocom Health History Questionnaire asks questions in Spanish...

provides answers in English

- | | |
|--|--|
| 1. ¿Le molestan coyunturas o músculos rígidos o dolorosos? | 1. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 2. ¿Se le hinchon las coyunturas? | 2. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 3. ¿Le molestan dolores en la espalda u hombros? | 3. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 4. ¿Le duelen los pies con frecuencia? | 4. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 5. ¿Esta deshabilitado en alguna manera? | 5. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 6. ¿Tiene algún problema con su piel? | 6. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 7. ¿Le pica o quema la piel? | 7. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 8. Sangra por largo tiempo cuando se hace una pequeña cortadura? | 8. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 9. ¿Se lastima fácilmente formando un cardenal o morete? | 9. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 10. ¿Se ha desmayado o se ha sentido como que se va a desmayar? | 10. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 11. Tiene alguna parte del cuerpo siempre adormecida? | 11. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 12. Ha tenido alguna vez convulsiones? | 12. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 13. Le ha cambiado últimamente su letra al escribir? | 13. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 14. Tiene tendencia a temblar o menearse mucho? | 14. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 15. ¿Se pone nervioso en presencia de personas extrañas? | 15. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 16. ¿Se le hace difícil tomar decisiones? | 16. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 17. ¿Se le hace difícil concentrar o recordar? | 17. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 18. ¿Se siente solo o deprimido? | 18. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 19. ¿Llora a menudo? | 19. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 20. Diría usted que tiene una perspectiva indefinible? | 20. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 21. Tiene dificultad en relajarse o reposarse? | 21. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 22. Tiende a preocuparse demasiado? | 22. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 23. Le molestan o asustan algunos sueños o pensamientos? | 23. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 24. ¿Tiende a ser tímido o sensitivo? | 24. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 25. ¿Se molesta mucho cuando lo critican? | 25. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 26. Pierde el genio con frecuencia? | 26. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 27. ¿Cosas pequeñas lo hacen molestar? | 27. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |
| 28. ¿Le molesta cualquier trabajo o problemas familiares? | 28. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 29. ¿Tiene algún problema con su vida sexual? | 29. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 30. ¿Ha considerado alguna vez suicidarse? | 30. Sí <input type="checkbox"/> No <input checked="" type="checkbox"/> |
| 31. ¿Ha deseado alguna vez o buscado ayuda psicológica? | 31. Sí <input checked="" type="checkbox"/> No <input type="checkbox"/> |

13. MUSCULOSKELETAL

- ☒ aching muscles or joints
- ☐ swollen joints
- ☒ back or shoulder pains
- ☐ painful feet
- ☐ handicapped

14. SKIN

- ☐ skin problems
- ☐ itching or burning skin
- ☐ bleeds easily
- ☐ bruises easily

15. NEUROLOGICAL

- ☐ faintness
- ☒ numbness
- ☐ convulsions
- ☐ change in handwriting
- ☐ trembles

16. MOOD

- ☒ nervous with strangers
- ☒ difficulty making decisions
- ☒ lack of concentration or memory
- ☐ lonely or depressed
- ☐ cries often
- ☐ hopeless outlook
- ☒ difficulty relaxing
- ☒ worries a lot
- ☐ frightening dreams or thoughts
- ☐ shy or sensitive
- ☒ dislikes criticism
- ☒ loses temper
- ☒ annoyed by little things
- ☐ work or family problems
- ☐ sexual difficulties
- ☐ considered suicide
- ☒ desired psychiatric help

When your patient speaks little English and your Spanish is limited or nonexistent, you need the new ROCOM Health History Questionnaire (Spanish).*

The uniqueness of this new ROCOM system lies in the fact that the questions are asked in *Spanish*, but you read the answers in *English*. The form itself does the "translating."

You have to see it yourself to appreciate the ease and completeness of this new history-taking technique, which includes 129 questions covering all body systems.

*Created and developed by Patient Care Systems, Inc.

For information about the new Rocom Health History Questionnaire (Spanish) and other components in the Rocom Medical Management System, please fill out the coupon and send it to us.

Name

Specialty

Address

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DYAZIDE®

Each capsule contains 50 mg. of Dyrenium®
(brand of triamterene) and 25 mg. of hydrochlorothiazide.

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CAN STOP POTASSIUM DEPLETION BEFORE IT STARTS

WITH NO SACRIFICE OF THIAZIDE EFFECTIVENESS

Before prescribing, see complete prescribing information in SK&F literature or *PDR*.

***Indications:** Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis,

and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules.

SK&F CO.

Carolina, P.R. 00630

a subsidiary of Smith Kline & French Laboratories

IN EDEMA*—IN HYPERTENSION*

ASOCIACION MEDICA DE PUERTO RICO

SEPTUAGESIMA
ASAMBLEA ANUAL



NOVIEMBRE 15 - 18, 1972

HOTEL SAN JUAN
ISLA VERDE
SAN JUAN, PUERTO RICO

NOTAS DE INTERES

- * **INSCRIPCION:** Los Miembros Activos pagarán \$10.00 (los Miembros Afiliados \$5) para participar en los actos científicos y sociales de la Asamblea. Los médicos no asociados pagarán \$50.00 por el mismo concepto.
- * **DISTINTIVO:** Se dará un distintivo a cada persona con derecho a asistir a todos los actos; este distintivo debe conservarse para ser usado en todo momento dentro del área de la convención.
- * **HORARIO DEL PROGRAMA:** Toda reunión, toda conferencia, todo acto en el programa empezará y terminará a la hora programada. Urge llegue a tiempo.
- * **BANQUETE ANUAL:** Obtenga con tiempo sus boletos para el Banquete-Baile-Show, que se celebrará el sábado 18 de noviembre, a las 8:00 p.m., en el Salón Isla Verde donde también habrá un coctel a las 7:30 p.m.
- * **EXHIBICIONES TECNICAS:** Las firmas expositoras cooperarán al éxito de nuestra Convención. Cordialmente le exhortamos a visitar cada una de las exhibiciones técnicas instaladas en el hotel.
- * **LLAMADAS DE EMERGENCIA:** El Telephone Answering Service, como una cortesía a la profesión médica, instalará un teléfono especial en el hotel (No. 791-1370) para atender llamadas de emergencia, que se avisarán por proyector en el salón de conferencias. Comuníquese con la operadora de dicho teléfono tan pronto llegue, para facilitar este servicio.
- * **AREAS DE ESTACIONAMIENTO:** Debido a que el local de estacionamiento es algo limitado, instamos a que se usen también otras áreas de la vecindad o que se deje el automóvil en la casa u oficina.

RECONOCIMIENTO

A los siguientes compañeros, quienes cumplen este año su trigésimo aniversario como miembros de nuestra Asociación, por sus nobles y desinteresadas ejecutorias en el desempeño de su profesión y por su elevado espíritu cívico y su gran interés en los problemas médicos del país:

JOSE A. AYBAR, MD
SALVADOR BUSQUETS, MD
ROBERTO BUXEDA, MD
PEDRO DURAND, MD
HERMAN FLAX, MD
JORGE GARCIA BIRD, MD
JOSEFINA GUARCH DE FLAX, MD
J. A. HERNANDEZ MATOS, MD
R. MALDONADO QUIÑONES, MD
CEFERINO MENDEZ POLO, MD
LUIS MONTALVO DURAND, MD
D. O. ROJAS DAPORTA, MD
LUIS A. SALIVIA, MD



IN MEMORIAM

Nuestro humilde, pero sincero homenaje de recordación para los compañeros fallecidos este año, y la más ferviente oración por sus almas.

VICTOR L. BIENES JIMENEZ, MD
VICTOR CARDONA ROBLES, MD
MARVIN S. CASHION, MD
RAFAEL FRANCO SANTIAGO, MD
PABLO MORALES OTERO, MD
F. L. RAFFUCCI, MD
U. LOPEZ SANABRIA, MD
A. GARCIA UBARRI, MD
ARSENIO VALLECILLO, MD
CHARLES E. WOLF SILVA, MD

EXHIBICIONES CIENTIFICAS

En el Parlor "A" del Salón Isla Verde

MORPHOLOGICAL STUDY OF LYMPH NODE IMPRINTS

E. Vélez García, MD
Jean Fradera, BS, MT

SUPINE HYPOTENSION SYNDROME — PHYSIOLOGIC VS. PHARMACOLOGIC MANAGEMENT

S. Colón Morales, MD

AMNIOGRAFIA Y PLACENTOGRAFIA

Heriberto Pagán Sáez, MD

PROBLEM ORIENTED RECORD

Elí A. Ramírez, MD

EDUCACION MEDICA CONTINUADA - "Cómo se Prepara una Conferencia"

División Audiovisual
División Educación Médica Continuada
Escuela de Medicina UPR
Recinto de Ciencias Médicas

COMBINED STEROID ANTI INFECTIVE TOPICAL THERAPY IN COMMON DERMATOSSES

R. Neal Scheiderman, MD

PROGRAMA MEDICO REGIONAL

Miércoles, 15 de noviembre

*Salón Isla Verde
Sección "B"*

Cursos de Mejoramiento Profesional en:

- Evaluación de Crecimientos Anormales
- Epilepsia
- Condiciones Pediátrico-Respiratorias

SESION DE LA MAÑANA

8:00 Matrícula

8:30 La Evaluación de Masas Tumorales

Discusión a Panel: *Isidro Martínez, MD*
Enrique Vélez García, MD
Pedro Juan Santiago, MD
Rafael Sorrentino, MD
Norman Maldonado, MD

11:00 Café

Simposio de Epilepsia (*Auspicio: Sección de Neurología, Escuela de Medicina UPR - Sociedad Puertorriqueña de Ayuda al Epiléptico*)

Preside: *Carlos E. Girod, MD*, Decano Escuela de Medicina

11:15 Clasificación Epidemiológica de las Epilepsias - *A. B. Baker, MD*

11:55 Correlación Clínica y Electrográfica del Tratamiento de la Epilepsia
Richard Harner, MD

12:35 Almuerzo

SESION DE LA TARDE

Actualidades Pediátricas Respiratorias

2:00 Asma Bronquial en el Niño

Ramón Casanova, MD
Angel Rivera, MD

2:30 Estudio Descriptivo Sobre Asma Bronquial en Niños
Manuel Soto Viera, MD

3:00 Fibrosis Quística del Páncreas
Pedro Mayol, MD

3:30 Tuberculosis en el Niño
Efraín Alicea, MD

PROGRAMA CIENTIFICO*Jueves, 16 de noviembre de 1972**Hotel San Juan
Salon Baron's*

Moderador: Roberto Rodríguez, MD

- 9:00 am EXAMINATION OF THE URINE SEDIMENT
George Schreiner, MD
- 9:40 am A PROGRESS REPORT ON 4,500 HEMODIALYSIS
Oswaldo Ramírez Muxó, MD
Rafael E. Ramírez González, MD
José L. Cangiano, MD
José A. Campos, MD
Jaime García Saavedra, MD
- 10:00 am ADJUSTMENT REACTION TO CHRONIC HEMODIALYSIS TREATMENT
Jaime García Saavedra, MD
- 10:20 am SIMPLIFIED METHODS FOR RENAL PRESERVATION
E. A. Santiago Delpín, MD
M. F. Mozes, MD
A. Moberg, MD
R. A. Campos, MD
J. S. Najarian, MD
- 10:40 am TOXIC NEPHROPATHY
George Schreiner, MD
- 11:20 am SERUM RENIN AS A DETERMINANT OF TREATMENT IN HYPERTENSIVE DISORDERS
J. A. Campos, MD
José L. Cangiano, MD
E. Waddell, BS
R. Ramírez González, MD
O. Ramírez-Muxó, MD
- 11:40 am VARIATIONS IN HEMATOCRIT LEVELS IN HEMODIALYZED PATIENTS WITH HEPATITIS
Rafael R. Ramírez González, MD
José L. Cangiano, MD
José A. Campos, MD
Oswaldo Ramírez Muxó, MD
- 12:30 pm ALMUERZO - Salón Tropicoro

*Jueves, 16 de noviembre de 1972**Hotel San Juan
Salón Isla Verde
Sección "B"*

SECCION DE MEDICINA INTERNA

- 9:00 am TROPICAL SPRUE: CLINICAL AND LABORATORY ASPECTS
José J. Corcino, MD
Frederick A. Klipstein, MD
Juan T. Tomasini, MD
Norman Maldonado, MD
- 9:20 am THE NBT RESPONSE IN INFECTIOUS DISEASE — A CLINICAL STUDY
Ramón H. Bermúdez, MD
Aida Fernández, MT
Rodrigo Menéndez Corrada, MD
- 9:40 am DEMAND PACING IN SINUS NODE BRADYARRHYTHMIAS
Jaime R. Cortés, MD
Elí A. Ramírez, MD
- 10:00 am SOCIAL FACTORS, INCIDENCE OF DIAGNOSIS, AND SYMPTOMS OF CORONARY HEART DISEASE
Gerald T. Perkoff, MD
- 10:40 am INCIDENCIA DE RESISTENCIAS PRIMARIA Y SECUNDARIA DE LA TUBERCULOSIS EN PUERTO RICO — SU SIGNIFICADO
Ramón E. Figueroa Lebrón, MD
Michael Zack, MD
- 11:00 am PRIMARY HYPERPARATHYROIDISM — REPORT OF A CASE CAUSED BY A 113-GRAM ADENOMA
Julián Vázquez Phard, MD
Lillian Haddock, MD
E. Vázquez Quintana, MD
Juan Velázquez, MD
- 11:20 am WATER AND ELECTROLYTE TRANSPORT IN TROPICAL SPRUE
José J. Corcino, MD
Milagros Maldonado, MD
- 11:40 am TRATAMIENTO QUIRURGICO DE LA INSUFICIENCIA CORONARIA
Leo Cuello, MD
- 12:30 pm ALMUERZO - Salón Tropicoro

Jueves 16 de noviembre de 1972

Hotel San Juan
Salón Isla Verde
Sección "C"

SECCION DE UROLOGIA

- Moderador: *Angel L. Ayala, MD*
- 9:00 am DIVERTICULUM FEMALE URETHRA
R. Machado, MD
R. Fortuño, MD

9:30 am SUPRABUBIC VESICO-URETHRAL SUSPENSION FOR THE CORRECTION OF STRESS INCONTINENCE

B. González Flores, MD
C. Maestre, MD
R. Santiago Correa, MD
L. N. Rodríguez Torres, MD

10:00 am MANAGEMENT OF MICROPHALLUS

Frank Hinman, MD

10:30 am RADICAL NODE DISSECTION AND CHEMOTHERAPY FOR TESTIS TUMORS

Harry Grabstald, MD

11:00 am PRINCIPLES FOR ESTABLISHMENT OF BACTERIA IN BLADDER AND KIDNEY

Frank Hinman, MD

11:30 am INTERSTITIAL RADIATION THERAPY FOR PROSTATIC CANCER

Harry Grabstald, MD

12:30 pm ALMUERZO - Salón Tropicoro

Moderator:

Félix S. Vilella Suau, MD

2:00 pm NATIONAL HEALTH PROGRAM AS SOME OTHER EXPERIENCES RELATED TO OUR FUTURE

George Silver, MD

2:30 pm PREPAID MEDICAL CARE (E.F.) - FACTS AND FALLACIES (S. T.) - THE EXPERIENCE OF THE WASHINGTON UNIVERSITY HEALTH PLAN

Gerald T. Perkoff, MD

3:00 pm PANEL DISCUSSION

Viernes, 17 de noviembre de 1972

Hotel San Juan
Salon Baron's

Moderador:

Pedro Mayol, MD

9:00 am CARDIOVASCULAR FINDINGS IN THE NOONAN SYNDROME

Héctor L. Rodríguez Fernández, MD
Barbara B. Bell, MD
Richard D. Rowe, MD

9:20 am PHOTOTHERAPY FOR NEONATAL JAUNDICE

Carmen A. Torres de Vega, MD
Marta Valcárcel, MD
Rafael Zapata, MD

- 9:40 am GROWTH HORMONE DEFICIENCY IN PUERTO RICAN CHILDREN
Ana Rodríguez, MD
Carmen A. Sáenz, MD
Carlos Cintrón, MD
María A. Toro, MD
- 10:00 am CONTINUOUS NEGATIVE CHEST WALL PRESSURE FOR RESPIRATORY DISTRESS SYNDROME
Marta Valcárcel, MD
Rafael Zapata, MD
Pedro Mayol, MD
- 10:20 am GOITER AMONG PUERTO RICAN CHILDREN
Carmen A. Sáenz, MD
Ana A. Rodríguez, MD
José A. Martínez, MD
María A. Toro, MD
- 10:40 am EFFECT OF DELAY IN CARE ON THE FATALITY RATE FROM TRAFFIC ACCIDENTS
Stefan H. Fromn, MD
Gustavo A. Escalera, MD
- 11:00 am SUITS AGAINST PHYSICIANS IN THE CASE LAW OF PUERTO RICO
John L. Simon, MD, LL.B
- 11:20 am EVALUATION OF TEACHING
Egidio S. Colón Rivera, MD
- 11:40 am ARGON LASER PHOTOCOAGULATION IN DIABETIC RETINOPATHY
José A. Berrocal, MD
Antonio Ramos, MD
- 12:30 pm ALMUERZO - Salón Tropicoro

Viernes, 17 de noviembre de 1972

Hotel San Juan
Salón Isla Verde
Sección "B"

Moderador: *Enrique Pérez Santiago, MD*

- 9:00 am SERIOUS INFECTION FOLLOWING SPLENECTOMY FOR STAGING OF HODGKIN'S DISEASE
E. Vélez García, MD
M. Ravry, MD
N. Maldonado, MD
J. Montalvo de Torres, MD
P. J. Santiago, MD

- 9:20 am EXPLORATORY LAPAROTOMY AND SPLENECTOMY FOR STAGING OF
HODGKIN'S DISEASE
P. J. Santiago, MD
E. Vélez García, MD
R. Sorrentino, MD
V. Gutiérrez, MD
J. Velázquez, MD
A. Frías, MD
- 9:40 am ASSESSMENT OF VITAMIN B12 ABSORPTION IN TROPICAL SPRUE UTILIZING
A WHOLE BODY COUNTER
José J. Corcino, MD
René C. Dietrich, MD
Aldo E. Lanaro, MD
- 10:00 am HYPERGLOBULINEMIC PURPURA
Norman Maldonado, MD
Antonio J. Grillo, MD
José Lozada, MD
- 10:20 am TOTAL THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN YOUNG
PATIENTS
Irma Ramírez, MD
Víctor Marcial, MD
Pedro J. Santiago, MD
Norman Maldonado, MD
Antonio Frías, MD
- 10:40 am RIESGO DE DESARROLLAR CANCER DEL CUELLO DE LA MATRIZ EN LAS
MUJERES CON MARIDOS QUE DESARROLLAN CARCINOMA EPIDERMIOIDE
DEL PENE
Isidro Martínez, MD
- 11:00 am SEPTIC ARTHRITIS DUE TO VIBRIO ESTORKENS, A CASE REPORT
W. Mercado Rosso, MD
M. A. Medina, MD
J. Lewis, MD
R. H. Bermúdez, MD
- 11:20 am HISTOPLASMA CAPSULATUM GRANULOMA IN BRAIN AND DIFFUSE ME-
NINGITIS – REPORT OF A CASE AND REVIEW OF THE LITERATURE
Rafael Borrás, MD
Rosa E. Fiol, MD
María Castillo, MD
- 12:30 pm ALMUERZO - Salón Tropicoro

SESION ABIERTA A MEDICOS Y
ABOGADOSSección "C"
Salón Isla Verde

2:00 pm Programa en coordinación con el Colegio de Abogados.

Conferenciante Invitado:

Lic. Melvin Belli

Moderadores:

Félix S. Vilella Suau, MD

Lic. Efrén Bernier

Viernes, 17 de noviembre de 1972

*Hotel San Juan
Sección "C"*

Moderador:

Alfred Axtmayer, MD

9:00 am RECENT ADVANCES IN THE SURGICAL MANAGEMENT OF RHEUMATIC DISEASES

Carlos Grovas, MD

Alejandro E. Franco, MD

Aníbal Lugo, MD

9:20 am TOTAL HIP REPLACEMENT ARTHROPLASTY

James R. Lewis, MD

9:40 am ROLE OF THE MICROVASCULATURE IN THE STROMAL COMPONENT OF CHRONIC CYSTIC MASTITIS

Robert Zeppa, MD

10:20 am INTRACRANIAL ANEURYSMAL SURGERY AT PUERTO RICO MEDICAL CENTER – MORBIDITY AND MORTALITY

Roberto A. Negrón, MD

José A. Alvarez de Choudens, MD

Nathan Rifkinson, MD

Pedro J. Borrás, MD

Boston Martin, MD

Hiram Mercado, MD

10:40 am DIVERTICULOSIS DEL COLON –TRATAMIENTO ACTUAL DE SUS COMPLICACIONES

Antonio Rodríguez Díaz, MD

11:00 am CIRUGIA ARTERIAL DIRECTA (Auspicio Asoc. Puertorriqueña de Graduados en Universidades Españolas)

Santiago Tamames, MD

11:40 am INTRABRONCHIAL BALLOON OCCLUSION AS TREATMENT IN MASSIVE PNEUMOTHORAX, PERSISTENT AIR LEAK AND BRONCHO-PLEURAL FISTULA

Olga Rodríguez, MD

Jorge O. Just Viera, MD

12:30 pm ALMUERZO - Salón Tropicoro

Viernes, 17 de noviembre de 1972

Cecilia's Place Hotel

SECCION UROLOGIA AMPR

Moderador: *Tomás Acevedo, MD*

9:00 am CARCINOMA OF PENIS WITH SKIN METASTASIS

*L. Nieves, MD**V. Torres, MD**A. Shapiro, MD*

9:30 am THE CAUSE OF URETRAL OBSTRUCTION IN PATIENTS WITH CARCINOMA OF THE CERVIX FOLLOWING RADIOTHERAPY

*B. González Flores, MD**Hugo Benítez, MD**Eugenio Feo, MD**Eileen T. Méndez, MD**A. R. del Toro, MD*

10:00 am GENITOURINARY ALTERATION AFTER LUMBAR SYMPATHECTOMY

*L. Nieves, MD**I. Gerena, MD**R. Fortuño, MD*

10:30 am LYMPHOMA OF THE TESTIS: CASE REPORT

*B. González Flores, MD**A. Ramírez Costa, MD**L. N. Rodríguez Torres, MD**Carlos C. Maestre, MD*

11:00 am REPAIR OF VESICAL EXSTROPHY

Frank Hinman, MD

11:30 am TUMORS OF THE RENAL PELVIS

Harry Grabstald, MD

12:00 m. AFFAIRS OF THE AMERICAN UROLOGICAL ASSOCIATION

W. E. Kiltredge, MD.

President

12:30 pm ALMUERZO - Salón Tropicoro

Sábado, 18 de noviembre de 1972

Hotel San Juan
Salón Baron's

SECCION DE OTORRINOLARINGOLOGIA

Moderador: *Alexis Fernández, MD*

- 9:00 am PROBLEMAS COMUNES DE OTORRINOLARINGOLOGIA DESDE EL PUNTO
DE VISTA DEL MEDICO DE FAMILIA
Alexis Fernández, MD
- 9:20 am PROBLEMAS DE OIDOS
Rex Bunker, MD
- 9:40 am PROBLEMAS DE NARIZ, GARGANTA Y SENOS PARANASALES
Arnaldo Pérez Vega, MD
- 10:00 am PROBLEMAS DE BRONQUIOS Y ESOFAGO
Rafael Rivera García, MD
- 10:20 am PANEL SOBRE TONSILECTOMIA Y ADENOIDECTOMIA
José Picó, MD
- 1:30 pm ALMUERZO - TOMA DE POSESION

Sábado, 18 de noviembre de 1972

*Hotel San Juan
Salón Isla Verde
Sección "B"*

SECCION DE MEDICINA FISICA Y REHABILITACION

Moderador: *Luis J. Flores Vilar, MD*

- 9:00 am GENERALIDADES DE LAS INCAPACIDADES
Cándido Martínez, MD
Luis J. Flores Vilar, MD
- 9:20 am CONSIDERACIONES SOBRE LA FIJACION DE INCAPACIDADES EN LOS
DESORDENES EMOCIONALES
Ramón Alonso Santiago, MD
- 9:40 am NEUROPATIA Y MIOPATIA DIABETICA
Rafael Berríos Martínez, MD
- 10:00 am PROYECCIONES SOBRE EL FUTURO DE LA REHABILITACION EN LOS
SERVICIOS DE SALUD EN PUERTO RICO
Carlos Armstrong Ressay, MD
- 10:20 am CONDUCTION VELOCITY IN UREMIC PATIENTS
Andrés Rodríguez, MD
Benigno Fernández, MD
Herman Flax, MD
- 10:40 am PROBLEMAS COMUNES DE REHABILITACION Y CIRUGIA DE MANO
Ramón Isales, MD

1:30 pm ALMUERZO – TOMA DE POSESION

Sábado, 18 de noviembre de 1972

Hotel San Juan
Salón Isla Verde
Sección "C"

Moderador: *Norman Maldonado, MD*

9:00 am EVALUATION AND TREATMENT OF PATIENTS WITH PORTAL HYPERTENSION

Robert Zeppa, MD

9:40 am CIRUGIA DE LA ESTENOSIS MITRAL

Santiago Tamames, MD

(Auspicia: Asociación Puertorriqueña de Graduados en Universidades Españolas)

10:20 am ADVANCES IN THE TREATMENT OF LYMPHOMA-COMBINATION CHEMOTHERAPY

George P. Canellos, MD

(Auspicia: Sociedad Puertorriqueña de Hematología)

11:00 am CONFERENCIA MAGISTRAL "DR. RAMON J. SIFRE"

ULCERATIVE COLITIS VERSUS CHRONN'S DISEASE OF THE COLON OR WHATEVER

Henry L. Bockus, MD

Presentación a cargo de: Adán Nigaglioni, MD. - Rector Recinto de Ciencias Médicas de la Universidad de Puerto Rico

(Auspicia: Sociedad Puertorriqueña de Gastroenterología)

12:00 m CONFERENCIA ANUAL "DR. RAMON M. SUAREZ"

RISK FACTORS FOR SUDDEN DEATH

William A. Sodeman, MD

Presentación a cargo de: Dwight Santiago Stevenson, MD.

(Auspicia: The Purdue Frederick Company)

1:30 pm ALMUERZO – TOMA DE POSESION

RESUMENES DE TRABAJOS PRESENTADOS EN EL PROGRAMA CIENTIFICO

A PROGRESS REPORT ON 4,500 HEMODIALYSIS.

Oswaldo Ramírez-Muxó, MD, Rafael E. Ramírez-González, MD, José L. Cangiano, MD, José A. Campos, MD and Jaime García-Saavedra, MD, Renal Section, San Juan Veterans Administration Center, San Juan, P. R.

In 26 months, more than 4,500 hemodialysis have been performed on 35 patients, 8 died, 27 are alive. Of this last group, 18 are veterans and 9 are non veterans admitted to the program under a hemodialysis sharing agreement between the Department of Health, the School of Medicine, and the Veterans Administration. Five patients and their spouses have been trained and placed home under our Home Hemodialysis Program.

Six patients have developed evidence of secondary hyperparathyroidism and one has undergone subtotal parathyroidectomy. Nine patients sustained elevated transaminases without hyperbilirubinemia. Four liver biopsies corroborated the impression of hepatitis. Only one patient's serum was positive for Australian Antigen. One Patient required the implantation of a permanent pacemaker due to complete A-V block. Transfusion requirements have been markedly reduced and hematocrits are running higher after the discontinuation of the use of the Kiil dialyzer and reduction of blood sampling. Of the 27 patients, 3 are inactive and not rehabilitated, while 24 are fully active. Fourteen of these patients are either working or studying.

ADJUSTMENT REACTION TO CHRONIC HEMODIALYSIS TREATMENT.

Jaime García-Saavedra, MD, Staff Psychiatrist, Renal Section, San Juan Veterans Administration Hospital, San Juan, P. R.

The expected and frequent reactions of patients with chronic renal failure to chronic hemodialysis treatment is a depression. How they deal with this depression to make a better adjustment is related directly, however, to their personality structure and their ego strength. There is a strong denial mechanism during the whole adjustment period. Usually this period of adjustment goes thru 3 stages:

1st Stage — of Uncertainty — where there is a marked anxiety and a deep depression built up as the initial response to their renal condition.

2nd Stage — of Gratefulness — where the anxiety is relieved by the acceptance of the patient to the program. They turn cooperative, sometimes "euphoric" like and with frequent fantasies.

3rd Stage — of Acceptance — where the reality is accepted and there is a resolution of the conflict.

SIMPLIFIED METHODS FOR RENAL PRESERVATION.

E. A. Santiago-Delpín, MD, M. F. Mozes, MD, A. Moberg, MD, R. A. Campos, MD and J. S. Najarian, MD., Department of Surgery, University of Minnesota.

The development of reliable renal preservation techniques has resulted in better utilization of cadaver organs for transplantation. Most available systems utilize cold oxygenated homologous plasma, recirculated in machines of varying complexity. We have attempted to simplify the perfusion process, by modifying its different aspects. A small compact, transportable perfusion machine was developed, and comparison with other established systems was performed by using 24-hour preservation of canine kidneys followed by reimplantation and contralateral nephrectomy. Survival was almost identical in all groups. Fifty-two human kidneys were then perfused in this machine, and of these, 47 were transplanted, with a 98 percent return to normal function (82 percent immediate). The problem of warm-ischemic damage was tackled next, and dog survival was measured after re-implantation of ischemically-damaged 24-hour preservation kidneys, protected by various drugs. Solumedrol (30 mg/kg) was found to improve survival from 30 to 100 percent if given i.v. before the ischemia, or if used in the perfusate. This prompted its use in all our cadaver donors in the clinical service. Finally, we attempted to simplify the perfusate, since the preparation of homologous plasma is a laborious process. Tris Buffer was found to maintain a constant pH eliminating the need for CO₂ and air. Albumin solution resulted in a 70 percent 2-week normal function vs. 90 percent using plasma as per-

fusate in the 24-hour model. Plasma is more reliable, but albumin is more convenient, and its use together with Solumedrol and Tris may improve it. These changes have simplified some of the aspects of kidney preservation.

SERUM RENIN AS A DETERMINANT OF TREATMENT IN HYPERTENSIVE DISORDERS.

J. A. Campos, MD, J. Cangiano, MD, E. Waddell, BS, R. Ramírez-González, MD and O. Ramírez-Muxó, MD, Renal Section, Veterans Administration Hospital, San Juan, P. R.

The role of the renin-angiotensin system has been thoroughly investigated in various hypertensive disorders. Renal hypertension can be associated with hyperreninemia for which corrective surgery has been successful. Adrenal hypertension, adenoma or hyperplasia, can be associated with hyporeninemic states for which surgery and/or specific medical therapy is recommendable. Our presentation will cover our present experience at the Veterans Administration Hospital with both hyper and hyporeninemic states. Clinical cases of hyperreninemia associated with both end stage renal disease and renal artery stenosis, and hyporeninemia associated with both excessive aldosterone levels and a normoaldosterone state will be described. The results of both surgical and medical therapy will be presented.

VARIATIONS IN HEMATOCRIT LEVELS IN HEMODIALYZED PATIENTS WITH HEPATITIS.

Rafael E. Ramírez-González, MD, José L. Cangiano, MD, José A. Campos, MD and Osvaldo Ramírez-Muxó, MD, Renal Section, Veterans Administration Hospital, San Juan, P. R.

Since the initiation of our Chronic Hemodialysis Program on September 1970, we have treated 35 patients in terminal renal failure at the San Juan Veterans Administration Hospital's Hemodialysis Unit. Signs of liver injury have been observed in 5 of these patients manifested by alterations in SGOT, SGPT, LDH, and abnormalities in liver biopsy. Three of these 5 patients have shown a concomitant and spontaneous increase in the venous hematocrit which correlates with the period of liver injury. In one patient, the liver lesion has healed and his hematocrit has gone down to previous baseline levels. Hematologic evaluation suggests that this increase in hematocrit is due to an augmented erythropoiesis. The role of erythropoietin (EP) and its relation to liver damage in the production of

these observations is discussed.

TROPICAL SPRUE: CLINICAL AND LABORATORY ASPECTS.

José J. Corcino, MD, Frederick A. Klipstein, MD, Juan T. Tomasini, MD and Norman Maldonado, MD, Tropical Malabsorption Unit, Universities of Rochester and Puerto Rico.

Tropical sprue remains the most common malabsorption syndrome observed in Puerto Rico. In spite of the multiple investigations performed on this syndrome, many physicians still have difficulty in its recognition and diagnosis. During the past year we have had the opportunity of evaluating fifty patients with this condition. Studies have included d-xylose absorption; fat and nitrogen balance; complete hematological evaluation including bone marrow aspirates as well as serum B₁₂, folate and iron levels; vitamin B₁₂ absorption; jejunal biopsies and small bowel series. This presentation will summarize the results obtained in such patients in an attempt to further clarify the diagnostic criteria that should be utilized for the diagnosis of this syndrome.

THE NBT RESPONSE IN INFECTIOUS DISEASE — A CLINICAL STUDY.

Ramón H. Bermúdez, MD, Aida Fernández, MT and Rodrigo Menéndez-Corrada, MD, Medical Service, Veterans Administration Hospital and the University of Puerto Rico School of Medicine.

The NBT test is a laboratory procedure aimed at differentiating between active bacterial and viral infections. In the presence of significant bacterial infections, there is an increased spontaneous reduction of pale yellow nitro blue tetrazolium (NBT) in vitro. The test actually consists of counting 100-200 neutrophils from peripheral blood and determining the percentage of cells undergoing spontaneous reduction with the normal value being eleven (11) percent. The increased reduction of NBT occurs early in bacterial infections due to pyogenic organisms, nocardia species and malaria. It yields a normal response with pulmonary tuberculosis, but is significantly positive with dissemination. Chronic schistosomiasis yields a normal response, but in some cases of acute infestation, the response has been positive. Disseminated candidiasis and cryptococcal meningitis yields a positive response as well as colonic amebiasis with hepatic abscess. The response has been negative in cases of drug fever and disseminated spirochetal disease (Lues). The NBT response will be useful to the practicing physician in the differential diagnosis of acute abdominal conditions, bacteremic infectious endocarditis, drug

fevers and confusing cases of meningitis.

DEMAND PACING IN SINUS NODE BRADYARRHYTHMIAS.

Jaime R. Cortés, MD and E. A. Ramírez, MD, Medical Service, VA Hospital and Dept. of Medicine, UPR Medical School, San Juan, Puerto Rico.

Two patients with symptomatic sinus bradyarrhythmias are described. One had an old inferior myocardial infarction and the other one had angina pectoris and was a diabetic under treatment with oral hypoglycemic agents and diet.

The handling of these patients, including vagolytic agents and temporary pacing, will be described. A restorative response of the sinus pacemaker to artificial ventricular pacing was observed in both patients. This is attributed to increase in cardiac output and improvement of the coronary blood flow.

It is concluded that:

1. the response of the sinus pacemaker to artificial pacing should be determined in these cases.
2. a demand mode pacemaker is advisable when a positive restorative response is observed.

INCIDENCIA DE RESISTENCIAS PRIMARIA Y SECUNDARIA DE LA TUBERCULOSIS EN PUERTO RICO — SU SIGNIFICADO.

Ramón E. Figueroa-Lebrón, MD, Michael Zack, MD, Servicio de Medicina - Hospital de Veteranos, San Juan, P. R.

Estudios de sensibilidad fueron hechos en todos los cultivos positivos de M. Tuberculosis hallados en el Hospital de Veteranos de P. R. Noventa y cuatro por ciento (94 por ciento) de los organismos demostraban resistencia a una o más de las drogas antituberculosas usadas. La mayor parte de los organismos ocurrían en pacientes previamente tratados para Tuberculosis. Había sin embargo 22 por ciento con resistencia *primaria* a las drogas.

La incidencia tan alta de resistencia primaria en nuestros casos es un reflejo de resistencia adquirida en la comunidad la cual es a la vez un reflejo de que los pacientes no han tomado su medicación propiamente o su régimen fue inadecuado desde el principio.

Debido a la importancia del problema las autoridades pertinentes y los médicos deben tener presente las implicaciones de un tratamiento inadecuado en esta enfermedad.

PRIMARY HYPERPARATHYROIDISM — REPORT OF A CASE CAUSED BY A 113-GRAM ADENOMA.

Julián Vázquez Plard, MD, Lillian Haddock, MD, E. Vázquez Quintana, MD and Juan Velázquez, MD.

Primary hyperparathyroidism was diagnosed preoperatively in a 41-year old woman with marked hypercalcemia, hypophosphatemia and cystic bone lesions. At operation a large adenoma extending along the anterior mediastinum was removed, weighing 113 grams. Postoperatively, she developed symptomatic hypocalcemia. The parathyroid function was evaluated postoperatively by means of EDTA and calcium infusions. Immunoassay levels of parathormone prior to and following surgery will be presented. The tumor removed is the second largest parathyroid adenoma to be reported in the literature.

The histology of the tumor and the clinical course of the patient will be discussed.

WATER AND ELECTROLYTE TRANSPORT IN TROPICAL SPRUE.

José J. Corcino, MD and Milagros Maldonado, RN - Tropical Malabsorption Unit, Universities of Rochester and Puerto Rico and the General Clinical Research Center, University of Puerto Rico, School of Medicine.

The etiopathogenesis of diarrhea in tropical sprue remains undetermined. To this purpose, we have performed segmental jejunal perfusion studies in 10 tropical sprue and 8 control subjects. A statistically significant difference concerning water, sodium, chloride and d-xylose transport in the jejunum of subjects with tropical sprue was observed as compared to controls.

Thus, jejunal secretion of water and electrolytes into the small intestine of patients with tropical sprue may explain, at least partially, the diarrhea observed in this syndrome. Further clarification of the etiopathogenetic mechanisms involved in the induction of such a secretory process await further investigation.

TRATAMIENTO QUIRURGICO DE LA INSUFICIENCIA CORONARIA.

Leo Cuello, MD, San Antonio, Texas

El tratamiento quirúrgico de la insuficiencia coronaria es variado, consiste en implante de arteria mamaria interna, puente aorto coronaria con vena safena o arteria mamaria interna, y resección de aneurisma

ventricular.

Este trabajo representa 132 puentes aorto coronarios (simples, dobles y triples) ocho resecciones de aneurismas ventriculares y varios implantes de mamaria interna.

La mortalidad es de 1.3 por ciento. Se discutirán las indicaciones operatorias, análisis electrocardiográfico, enfermedades asociadas y varios detalles importantes sobre la técnica quirúrgica y cuidado postoperatorio.

CARDIOVASCULAR FINDINGS IN THE NOONAN SYNDROME.

Héctor L. Rodríguez-Fernández, MD, Barbara B. Bell, MD, and Richard D. Rowe, MD, Dept. of Pediatrics, Johns Hopkins Hospital and School of Medicine, Baltimore, Maryland.

The Noonan Syndrome (NS), otherwise known as the Turner phenotype is frequently associated with congenital heart disease. Twenty two patients with NS and congenital heart disease were studied by cardiac catheterization. As in previously published series, pulmonic stenosis (PS), isolated or in association with other defects was the predominant lesion (16 of 22). The physical, electrographic and radiological manifestations of PS in the NS differ from those of typical PS, hindering the ability of the clinician to predict the degree of obstruction and the associated lesion if any, prior to cardiac catheterization. In our 16 patients the post catheterization diagnoses were predicted accurately as follows: 2 of 7 with isolated valvar PS, 1 of 5 with PS and atrial septal defect and 4 of 4 with PS and ventricular septal defect. These findings suggest that clinical data, adequate in estimating severity and the presence or absence of associated lesions in typical PS, is not useful in the PS associated with the NS.

PHOTOTHERAPY FOR NEONATAL JAUNDICE.

Carmen A. Torres de Vega, MD, Marta Valcárcel, MD, Rafael Zapata, MD, Department of Pediatrics, University of Puerto Rico, School of Medicine.

Since 1958 phototherapy has been used for prevention and treatment of hyperbilirubinemia. *The products of photodecomposition of bilirubin have been demonstrated to be less toxic than bilirubin and readily excreted in the bile and urine. This form of therapy is one more resource in reducing the level of bilirubin.*

Phototherapy has been useful as adjuvant for the management of neonatal jaundice, however it should not be expected to be a substitute for exchange transfusion in patients whose bilirubin level present high

risk kernicterus. One should be on guard to avoid procrastination in cases requiring exchange transfusion.

Experience with one hundred hyperbilirubinemic newborns treated with phototherapy at the University Hospital will be discussed. Presentation will include data on indications, duration of therapy and complications.

GROWTH HORMONE DEFICIENCY IN PUERTO RICAN CHILDREN.

Ana A. Rodríguez, MD, Carmen Ana Sáenz, MD, Carlos Cintrón, MD, María A. Toro, MD, Department of Pediatrics, Endocrinology Section of San Juan City and University Hospitals.

Although the exact incidence of Growth Hormone deficiency among Puerto Rican children is not known we have in our clinic several patients with this diagnosis which merit our attention.

The purpose of this paper is to review the known cases of hypopituitarism in the Pediatric Endocrine clinic of Puerto Rico Medical Center in the past five years.

The use of radioimmunoassay tests now available to us have simplified the diagnosis of this entity. However, another major problem remains, and that is, the lack of adequate treatment for this type of growth failure. We hope to overcome this drawback, by engaging in research which will make Growth Hormone extract from human pituitaries available for these children.

CONTINUOUS NEGATIVE CHEST WALL PRESSURE FOR RESPIRATORY DISTRESS SYNDROME.

Marta Valcárcel, MD, Rafael Zapata, MD, Pedro Mayol, MD, Department of Pediatrics, University of Puerto Rico, School of Medicine.

Continuous positive airway pressure (CPAP) has shown to improve the oxygenation in infants with the respiratory distress syndrome and increase their survival rate. Chernick has demonstrated comparable results with the application of a continuous transpulmonary pressure by means of the infant incubator respirator with a simple modification to maintain continuous negative pressure to the chest wall. During the last six months (December 1971 to May 1972) fifteen cases received this form of therapy with seven survivals at the Neonatal Intensive Care Unit of the University Hospital. During the same period of time of the previous year (December 1970 to May 1971)

14 cases received intermittent positive pressure ventilation with 2 survivals. The use of continuous negative pressure has proven to be useful in the management of Respiratory Distress Syndrome in our institution.

GOITER AMONG PUERTO RICAN CHILDREN.

Carmen Sáenz, MD, Ana A. Rodríguez, MD, José A. Martínez, MD and María A. Toro, MD, from the Pediatric Department, Endocrinology Section, of the San Juan City Hospital and University Hospital.

A review was made of the patients with goiter seen at the Pediatric Endocrine Clinic of the San Juan City Hospital during the past four years. Prevalence of autoimmune thyroiditis, suppurative thyroiditis, congenital enzymatic defects, acute and subacute thyroiditis iodine and thyrotoxic goiters are discussed as well as new and current techniques of laboratory evaluation of these entities.

EFFECT OF DELAY IN CARE OF THE FATALITY RATE FROM TRAFFIC ACCIDENTS

Stefan H. Fromm, MD, Gustavo A. Escalera, MD.

During 1971 there were 561 fatalities as a result of highway accidents in Puerto Rico. The autopsy findings, the location of the accident, and the timeliness and adequacy of first aid and definitive treatment were reviewed. A scale of presumed salvageability, based on an estimate of the victims' chances for survival if estimable care were immediately available, was applied to each fatality. Over 30 percent of victims died of potentially salvageable injuries because of delay and/or non availability of adequate first aid and definitive treatment. Improvement of emergency medical services is a must.

SUITS AGAINST PHYSICIANS IN THE CASE LAW OF PUERTO RICO.

John L. Simon, MD, LLB

The case law as to suits against physicians in Puerto Rico is reviewed. The evolution of the principles governing the concept of malpractice and its ramifications are discussed. Certain interesting cases are analyzed.

EVALUATION OF TEACHING.

Egidio S. Colón-Rivera, MD, Department of Pediatrics, School of Medicine.

We are more involved all the time with Post Graduate

Medical Education and the Continuous Medical Education of the Physician. More and more is going to be done in this area, but we must be sure that we have accomplished our objectives. To be able to do this we must evaluate our results. Actual experiences in evaluating teaching in our "Curso de Perfeccionamiento" will be used as the main basis for this presentation.

ARGON LASER PHOTOCOAGULATION IN DIABETIC RETINOPATHY.

José A. Berrocal, MD and Antonio Ramos, MD

With the introduction of laser rays in ophthalmology, it has been possible for the first time, to obliterate newly formed vessels at the optic disc and near the macula.

This obliteration has reduced the frequency of vitreous hemorrhages in diabetic retinopathy and other vascular abnormalities. If the vitreous hemorrhages are not prevented, blindness results.

We will present our experience with this new and most exciting modality of photocoagulation.

SERIOUS INFECTION FOLLOWING SPLENECTOMY FOR STAGING OF HODGKIN'S DISEASE (H.D.).

E. Vélez-García, MD, M. Ravry, MD, N. Maldonado, MD, J. Montalvo de Torres, MD and P. J. Santiago, MD. Hematology Section, Department of Medicine, University of Puerto Rico School of Medicine.

Splenectomy as a diagnostic procedure and for accurate staging of H. D. and other lymphomas, is currently being employed in many centers. An increased frequency of serious infections, especially in the young, is known to occur in splenectomized patients within 2 years of operation. Fifty two patients with H. D. have had this procedure at the University Hospital in the past 2 years, as part of a carefully planned study; 18 of these have been 13 years of age or younger and 2 of them have had life-threatening infections within one year after splenectomy. One patient (a 13-year old girl) developed a severe episode of pneumococcal meningitis 8 months after the operation and the other patient (a 6-year old boy) developed Hemophilus meningitis 7 months after the operation. Rapid clinical improvement ensued in both only after aggressive antibiotic therapy was given. Three months later, the latter patient was re-admitted because of a febrile illness accompanied by severe abdominal pain.

Subsequently, the diagnosis of pneumococcal peritonitis was confirmed. After treatment with high doses of penicillin the patient also recovered from this episode uneventfully. *Although the possibility exists that these infections had no relation to splenectomy, children and adolescents with H. D. may be more prone to develop such infections and caution should be exercised against the indiscriminate use of laparotomy and splenectomy in these patients.* Serious infections are certainly part of the spectrum, as yet not entirely known, of late complications of this procedure. The role of the spleen in their etiology is not known and deserves further study.

EXPLORATORY LAPAROTOMY AND SPLENECTOMY FOR STAGING OF HODGKIN'S DISEASE (H.D.) IN CHILDREN.

P. J. Santiago, MD, E. Vélez-García, MD, R. Sorrentino, MD, V. Gutiérrez, MD, J. Velázquez, MD and A. Frías, MD, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

Curative treatment of H. D. depends on precisely staging the extent of disease prior to institution of therapy. The accuracy of the staging and thus, the curability rate has increased significantly with the use of more sophisticated techniques such as exploratory laparotomy. Although the latter procedure has been used frequently in adults, data are scarce in children. Exploratory laparotomy, splenectomy, liver and multiple lymph node biopsies were performed in 18 children (12 males, 6 females), whose ages ranged from 6 to 15, after the usual routine staging procedures were obtained. The histopathological diagnoses were: lymphocytic predominance in 4, mixed cellularity in 11, nodular sclerosis in 2 and lymphocytic depletion in 1. Lymphangiograms were attempted in 17 patients: 5 were +, 4 negative and 8 unsuccessful. Only 2 of the 5 + ones were confirmed at laparotomy and the 4 negative ones did not have disease in the retroperitoneal space but involvement was present elsewhere in the abdomen. Splenic involvement was suspected pre-operatively in 4 cases, but it was proven in only 2; whereas, it was found in 7 of the 14 in whom it was thought to be absent. Only 1 of 13 patients with hepatic abnormalities was proven to have liver involvement. After laparotomy, the staging was altered in 11 patients: 5 from II to III, 4 from III to II, and one each from I to II and from III to IV. We feel that laparotomy, with splenectomy, liver and multiple abdominal node biopsies, is essential for accurate staging and thus, for planning curative treatment of H. D. in children. No complications have been seen, but long term adverse

effects remain to be studied.

ASSESSMENT OF VITAMIN B₁₂ ABSORPTION IN TROPICAL SPRUE UTILIZING A WHOLE BODY COUNTER (Hematology Section, University Hospital).

José J. Corcino, MD, René C. Dietrich, MD and Aldo E. Lanaro, MD, Tropical Malabsorption Unit, Universities of Rochester and Puerto Rico and Puerto Rico Nuclear Center.

Vitamin B₁₂ malabsorption is one of the most consistent and persistent findings in tropical sprue. To date, most studies concerning B₁₂ absorption have been performed utilizing the Schilling test. The latter, though a relatively sensitive test, involves the parenteral administration of 1000 ug of vitamin B₁₂, usually resulting in clinical and hematological improvement. This precludes subsequent evaluation of the effect of other agents on the therapy of the disease.

A whole body counter, recently made available at the Puerto Rico Nuclear Center, has allowed us to study vitamin B₁₂ absorption utilizing small doses (0.5 ug) of the labeled vitamin. To date, 15 control and 15 tropical sprue subjects have been studied utilizing this technique. An excellent separation was obtained between both groups. Thus, this technique provides a useful tool for the study of the effect of different modalities of therapy in tropical sprue, without the need of administering pharmacological doses of vitamin B₁₂.

HYPERGLOBULINEMIC PURPURA.

Norman Maldonado, MD, Antonio J. Grillo, MD, José Lozada, MD, Heriberto Morales, MD and Rafael Rizek, Hematology Section, Department of Medicine, University of Puerto Rico School of Medicine.

Hyperglobulinemic Purpura was first described by Waldenström in 1948 and defined as a benign purpura of the lower extremities associated by marked hyperglobulinemia of the polyclonal type. *This rather uncommon disease was diagnosed in 5 patients at the Puerto Rico Medical Center.* All the patients were young females. The routine hematologic studies were normal. Rouleaux formation, increase sedimentation rate, polyclonal hyperglobulinemia and increase in all immunoglobulins were present. Skin biopsies were not diagnostic. There was a tendency to have other manifestations of autoimmune collagen diseases. One patient developed overt systemic lupus erythematosus, another developed Sjögren's syndrome with arthritis

and keratoconjunctivitis sicca and another patient has idiopathic leukopenia. One patient was treated with Imuran with some subjective improvement. Two patients received Thioguanine for several months without any benefit. Two patients required steroids because of complicating illnesses without benefit to the purpura. *Our experience suggest that this condition is closely related to other autoimmune disorders but has no relation with the malignant dysproteinemias.* Treatment is uniformly unsuccessful.

TOTAL THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN YOUNG PATIENTS.

Víctor Marcial, MD, Pedro J. Santiago, MD, Norman Maldonado, MD, Antonio Frías, MD. Departments of Pediatrics and Medicine, University of Puerto Rico School of Medicine.

Eleven male and three female patients aging 2 to 36 years admitted to the University District Hospital with acute lymphoblastic leukemia (ALL) agreed to be placed in an experimental regimen of therapy for that disease (Total Therapy For ALL). The treatment consisted of induction with Vincristine and Prednisone; therapy to the central nervous system with methotrexate intrathecally every 4 days for 5 doses, and irradiation to the cranial vault with 2,400 rads in 2 weeks, after completion of hematological remission; and continuation therapy with purinethol daily, and methotrexate and cyclophosphamide orally once weekly. The results of therapy in this group are as follows: twelve patients are in complete remission, five of them over one year after diagnosis, and two patients have had relapse of the disease. Complications of therapy have included: temporary alopecia, myelosuppression, and immunosuppression with frequent infections. Combined intensive chemotherapy along with radiotherapy to the CNS promises to produce long remissions in ALL in childhood and young adults, and some authors claim that some cures can be achieved.

RIESGO DE DESARROLLAR CANCER DEL CUELLO DE LA MATRIZ EN LAS MUJERES CON MARIDOS QUE DESARROLLARON CARCINOMAS EPIDERMÓIDE DEL PENE.

Isidro Martínez, MD, Programa Control del Cáncer, Departamento de Salud de Puerto Rico.

Este estudio fue conducido para buscar la frecuencia de carcinoma epidermoide del cuello de la matriz entre

las mujeres de 889 hombres con diagnóstico de carcinoma epidermoide del pene en Puerto Rico del 1950 al 1968, la secuencia e intervalos entre los dos diagnósticos, en comparación con otro grupo similar de varones con otros carcinomas y sus mujeres. Las mujeres del grupo de varones con carcinoma del pene desarrollaron 8 casos de carcinoma epidermoide de la matriz en contraste con ninguno del grupo control. Los carcinomas de la matriz fueron diagnosticados más tarde y en estadio más temprano que los correspondientes carcinomas del pene de sus maridos. Cuando se presente el Estudio esperamos incorporar 200 casos adicionales del 1968 al 1971 que se están estudiando.

SEPTIC ARTHRITIS DUE TO VIBRIO ESTORKENS, A CASE REPORT.

W. Mercado-Rosso, MD, M. A. Medina, MS, J. Lewis, MD, R. H. Bermúdez, MD, Department of Medicine, San Juan VA Hospital, San Juan, P. R.

Septic arthritis may be multicausal in etiology. Pyogenic cocci, treponema, brucella, salmonella, shigella, tuberculosis, and fungi are known etiologic agents. In some cases the causal organism is suspected and easily identified. This is the case report of a young Puerto Rican male, who was admitted four times to several hospitals in the San Juan area in the span of two years. His main complaints were Lt. hip pain, fever, night sweats, malaise, and weight loss.

Confusing past history of brucellosis and recent history of urethritis and conjunctivitis was given in the clinical history.

Clinical features, in addition to the radiographic findings were limited to a single joint.

Aspiration of the Lt. sacroiliac joint yielded 10 cc of serosanguineous fluid from which vibrio estorkens was isolated. Serial blood cultures were negative.

He was treated with one gram of tetracycline daily for two months with clinical and radiological improvement. Possible portal of entry of the organism were either oral or on intravenous route (drug addiction).

HISTOPLASMA CAPSULATUM GRANULOMA IN BRAIN AND DIFFUSE MENINGITIS. REPORT OF A CASE AND REVIEW OF THE LITERATURE.

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Very few cases of central nervous system involve-

ment by *Histoplasma capsulatum* have been reported in the literature. In Puerto Rico where the prevalence of histoplasmosis has been accepted at 15-30 percent, the majority of cases are benign and transient. In the rare fatal cases reported no CNS involvement has been described.

This report presents a fatal case of histoplasmosis in an 18-year old young man, undiagnosed in two admissions to the University Hospital. Three and a half months before death he was diagnosed as having a benign gastric ulcer. Neurological findings which will be discussed led to multiple tests which were all negative. He died on April 3, 1972 after a febrile, downhill course. Neurological and autopsy findings will be discussed. A brief review of the literature will also be presented.

RECENT ADVANCES IN THE SURGICAL MANAGEMENT OF RHEUMATIC DISEASES.

Carlos Grovas, MD, Alejandro E. Franco, MD, Aníbal Lugo, MD, Department of Orthopedic Surgery and Clinical Pharmacology Unit, University of P. R., School of Medicine.

The last 10 years have seen the advent of new surgical techniques for the management of rheumatic conditions. These new developments have provided the orthopedic surgeon with additional tools for helping the rheumatologists to deal with the progressive crippling of arthritis.

The hand, knees and hips, the most usually affected joints in arthritis, are the ones for which more surgical procedures have been developed. The Swanson sylastic prosthesis for replacement of the metacarpophalangeal joints have become the most impressive and promising procedure for re-establishing function to the arthritic hands. For the knees, the McKeever metal prosthesis for replacing the tibial plateau has been used with success specially in osteoarthritis of the knee. For arthritis of the hip, the most rewarding procedure is the Charnley type of total hip replacement.

It is the purpose of this paper to present the experience acquired during the last year by our group in performing these procedures. The indications and contraindications for such type of surgery and the necessity of a team work approach to deal with these patients, will be stressed.

TOTAL HIP REPLACEMENT ARTHROPLASTY.

James R. Lewis, MD, Veterans Administration Hospital, San Juan, P. R., Assistant Prof. Orthopedic Surgery, Univ.

P. R., School of Medicine.

The most promising development in Orthopedic Surgery for the treatment of the painful, stiff hip has been the Total Hip Replacement Arthroplasty, developed to its present stage in England. *I present a brief report on the development, biomechanics, indications for, and results to date of this procedure, based on an extensive review of the medical literature on this subject, and on my personal experience with this operation on thirteen (13) patients operated by me, here, in Puerto Rico.*

INTRACRANIAL ANEURYSMAL SURGERY AT PUERTO RICO MEDICAL CENTER. MORBIDITY AND MORTALITY.

Roberto A. Negrón, MD, José A. Alvarez de Choudens, MD, Nathan Rifkinson, MD, Pedro J. Borrás, MD, Boston Martín, MD, and Hiram Mercado, MD, Divisions of Neurosurgery, Department of Surgery, University of Puerto Rico School of Medicine and San Juan City Hospital.

Refinements in surgical skills and the use of the operating microscope coupled with better selection of patients, have led to a worldwide improvement in mortality and morbidity following surgery for cerebral aneurysms. We, at the Centro Médico, have been very fortunate in obtaining quite satisfactory results. We feel that most patients with symptomatic or ruptured aneurysms can be operated successfully and therefore prevent fatal rebleeding and the agony of uncertainty once a patient or his relatives know he harbors such a treacherous disease. *Statistics of our results are presented including factors as age, pre and post operative condition, time between rupture and surgery, etc....*

DIVERTICULOSIS DEL COLON - TRATAMIENTO ACTUAL DE SUS COMPLICACIONES.

Antonio Rodríguez-Díaz, MD, FACS

Se hace un estudio y presentación de Casos Clínicos Personales.

Diverticulitis Cecal y Apéndice.

Diverticulitis Aguda.

Obstrucción Intestinal por Diverticulitis o Cáncer.

Hemorragia Intestinal Masiva.

Perforación en cavidad libre o cubierta.

Morbilidad y Mortalidad.

Comentarios.

Bibliografía.

INTRABRONCHIAL BALLOON OCCLUSION AS TREATMENT IN MASSIVE PNEUMOTHORAX, PERSISTENT AIR LEAK AND BRONCHO-PLEURAL FISTULA.

Olga Rodríguez, MD and Jorge O. Just Viera, MD, from the University of Puerto Rico School of Medicine and the San Juan City Hospital.

Tension pneumothorax, persistent air leak, and bronchial pleural fistula are increasing problems in our geriatric population with obstructive airway disease. Classical treatment has been closed thoracotomy drainage and surgery. Continuous escape of air may be an impairing factor to healing and closure of the involved bronchi. Controlled intrabronchial occlusion was evaluated as therapeutic adjunct, in the treatment of these conditions.

Thirty dogs were equally divided into control and treated groups. Right upper and right diaphragmatic lobectomy, as well as right middle lobe partial amputation (hemilobectomy) were performed in three groups of five dogs each. All bronchi were left open. In the treated group, a catheter with an inflatable balloon was

placed in the trachea, with the distal cuffed end into the sectional bronchus. The proximal end was brought out through a small tracheal incision. Inflation of the balloon with water controlled the air leak.

Length of survival was measured from the removal of the intercostal tube, which was done immediately after the chest was closed. Most control animals died from tension pneumothorax in one hour or less and usually within 10 to 15 minutes. Two survived between one and twelve hours and only one survived more than 24 hours. All treated dogs survived 3 days or more, with complete control of the air leak. The main complication encountered, bronchial mucosal changes, should be avoidable clinically with periodic cuff deflation and appropriate cuff design. With the advent of bronchial burshing techniques, placement of the catheter should not be a problem.

This technique, used simultaneously with closed thoracotomy, promises to be a useful technique not only in the treatment of poor risk emphysematous patients, but also for significant postoperative air leak or bronchopleural fistula. The basic principle involved is control of the air leak which should result in earlier non operative bronchial closure.

TREATMENT OF DRUG RESISTANT HYPERTENSION IN CHRONIC KIDNEY DISEASE

José L. Cangiano, MD
Rafael Ramírez González, MD
Osvaldo Ramírez-Muxó, MD
Enrique Pijem, MD
Elaine Waddell, BS

The presence of severe hypertension in man is a medical emergency which frequently poses a formidable problem of management. In most instances severe hypertension may be promptly controlled by the judicious use of potent parenteral antihypertensive agents and consequently, prevent a major cardiovascular catastrophe. However, the clinician may occasionally encounter severely hypertensive patients with or without renal failure who demonstrate resistance to all known antihypertensive drugs.

The purpose of this paper is to present a severely hypertensive patient unresponsive to the use of potent parenteral antihypertensive drugs, including long term administration of the experimental drug diazoxide (Hyperstat) * and the effects of bilateral nephrectomy on blood pressure.

Case Report

First Admission:

A. R. M., a 36-year old male was transferred from San Juan City Hospital to the Veterans Administration Hospital on July 7, 1970 with complaints of dyspnea at rest, orthopnea, leg edema and decreased urinary output. Six years before admission he developed nephrolithiasis and recurrent bouts of pyelonephritis. At this time hypertension first appeared but was satisfactorily controlled by oral diuretics and alpha-methyl dopa. In 1965 a right nephrectomy was performed at another hospital because of recurrent calculous disease. Hypertension persisted and he was then followed for several years on antihypertensive medication. Four weeks before admission he began to develop symptoms of dyspnea at rest, orthopnea and leg edema. Oral digoxin was started but his condition did not improve. He was then admitted to Veterans

Administration Hospital after severe oliguria ensued.

The patient was an undernourished white male who was in severe respiratory distress, diaphoretic and pale. The temperature was 98.6° the pulse rate was 120, the respirations were 42 and the weight 120 lbs. The pupils were widely dilated and slowly reacting to light. A Grade II Keith Wagener hypertensive retinopathy was observed. The heart was enlarged with the apex at the anterior axillary line, and the rhythm was regular at a rate of 120 beats per minute. The liver span was percussed at 14 cm.; the spleen and kidneys were not felt. There was minimal ankle edema.

The hemoglobin was 12.5 grams percent, the hematocrit 37 percent, the white blood cell count was 11,600, 88 percent neutrophils, 9 percent lymphocytes and 3 percent bands. The urine was yellow clear with an acid pH. Specific gravity was 1.010, albumin 2+ and sugar was negative. Urinary sediment showed many white and red blood cells, hyaline casts and fine and coarse granular casts. The blood urea nitrogen was 57 mg., the creatinine 5.2 mg., the calcium 8.2 mg., the phosphorous 7.2 mg., the uric acid 14 mg., the total protein 6.1 gm., the albumin 2.9 gm., the globulin 3.2 gm., and the cholesterol 160 mg. per 100 ml. The sodium was 120 mEq., the potassium 6.0 mEq., the chloride 78 mEq., and the carbon dioxide 28 mEq. per liter. The glutamic oxalo acetic transaminase (SGOT) was 70 mu., the lactic dehydrogenase (LDH) 270 mu., creatine phosphokinase (CPK) 200 mu., and the alkaline phosphatase 100 milliunits per milliliter. An electrocardiogram showed left ventricular hypertrophy with strain and sinus tachycardia at a rate of 104 per minute. The x-ray films of the chest revealed marked cardiomegaly with bilateral infiltration. The urine culture showed an abundant growth of *Proteus ruttgeri* and *Paracolon*. The creatinine clearance was 11 milliliters per minute per 1.73 square meters and the 24 hour urinary protein was 1.6 grams. Random peripheral serum renin values were obtained twice and found to be elevated, 7.23 and 6.80 Goldblatt units $\times 10^{-4}$ per ml. (normal values are from 0 to 1.5). The initial treatment consisted of intramuscular reserpine, intravenous ampicillin and oral action exchange resin (Kayexalate). In addition a dose of 0.25 mg. of cedilanid was given intravenously. Despite this treatment the blood pressure remained elevated at a systolic of 220 and a diastolic of 170. A trimethaphan (Arfonad) drip with 1 to 2 mg. per milliliter of glucose in water, was started while the patient's position was tilted to 50° in a circular bed. The blood pressure began to drop when he developed severe mydriasis and blurring of vision. Trimethaphan was discontinued and intramuscular apresoline in doses of 10 to 20 mg. was then started. However, the blood pressure levels remained at 180 to 220 systolic and 130 to 150 diastolic.

The urinary output was maintained at a rate of 40 milli-

* Kindly supplied by L. Hobson, M. D., PH. D. Schering Labs., Bloomfield, N. J.

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liters per hour. The patient continued in a poor condition, obtunded with severe diarrhea and vomiting. Repeated serum electrolytes revealed a sodium of 123 mEq. per liter. One hundred seventy five milliliters of 5 percent sodium chloride was given to replenish sodium. His sensorium began to clear but his blood pressure remained elevated. At this time his serum sodium was 125 mEq. per liter. A peritoneal dialysis was started in an attempt to correct the electrolyte imbalance in the face of renal function impairment and congestive heart failure. Sixty milligrams of sodium nitroprusside were given intravenously without lowering the blood pressure. The experimental drug diazoxide was then given after obtaining the appropriate written informed consent. An initial dose of 300 mg. was administered intravenously and blood pressure decreased to 150 systolic, 90 diastolic. A repeated intravenous dose of 300 mg. of diazoxide was administered 6 hours later when the blood pressure began to escalate again. He was started on 50 mg. four times a day of hydralazine, 500 mg. four times a day of alphamethyldopa and 160 mg. a day of furosemide. A trial with guanethidine had to be discontinued because of paralytic ileus. His blood pressure decreased to 200/130 supine and 150/110 standing when diazoxide was combined with 10 to 20 mg. of parenteral pentolinium (ansolysen). Although his blood pressure was not completely controlled, his general condition gradually improved and on September 15, 1970 he was discharged on a 40 gm. protein diet with 4 gm. of sodium chloride and daily pentolinium injections of 10 to 20 mg. He was seen at weekly intervals at the Renal Clinic.

Second Admission:

On October 15, 1970 his blood pressure was again 210 systolic and 170 diastolic and was readmitted for the control of his blood pressure. He also complained of dyspnea at rest, orthopnea and nocturnal paroxysmal dyspnea.

On physical examination he was found with moderate dyspnea. The temperature was 98.2° F., the weight 120 lbs. the pulse 96/min., the respirations 24/ min. and the blood pressure 220/150, supine and 190/140 upright. The fundoscopic exam disclosed a Grade III Keith-Wagener hypertensive retinopathy. Crackling rales were heard on both bases and a soft systolic murmur was present at the apex. Otherwise the physical examination was non contributory.

The hemoglobin was 9.4 mg. percent, hematocrit 28.5 percent. The white blood cell count was 45,000; 73 percent neutrophils, 1 percent stab, 21 percent lymphocytes, 4 percent monocytes and 1 percent eosinophil. The urine was yellow clear, acid, with a specific gravity of 1.006, a 2+ albumin and negative for sugar. The urinary sediment showed 2 white blood cells per high power field. The blood urea nitrogen was 70 mg. percent, the glucose was 125 mg., the creatinine was 8.2 mg., the calcium was 9.6 mg., phosphorus 6.5 mg., the uric acid 14 mg., total protein 6.4 mg. and cholesterol 260 mg. per 100 ml. The serum sodium was 140 mEq., potassium 4.2 mEq., chloride 98 mEq. and carbon dioxide 28 mEq. per liter. The SGOT, LDH, CPK and the alkaline phosphatase were normal. The creatinine clearance was 7.1 milliliters per minute per 1.73 square meters of body surface. The urine culture was negative for organisms. The chest x-ray showed a slight infiltrate in the right cardiophrenic angle.

The patient was started on daily injections of diazoxide

in addition to the previous antihypertensive therapy. The daily dose of diazoxide ranged from 300 to 600 mg. The response to diazoxide was transient and usually lasted from four to ten hours. He received a total of 14 injections in 10 days. His blood pressure remained at levels of 220 systolic, 150 diastolic despite achieving dry weight. The patient went into frank congestive heart failure necessitating peritoneal dialysis for its relief, however, the blood pressure remained elevated. Removal of the remaining kidney and construction of an arteriovenous fistula were performed on November 4, 1970. The patient was started on hemodialysis. Three days after the nephrectomy the blood pressure decreased to 130/90 - 150/100 without the use of antihypertensive medications. Whenever the patient's weight increased between dialysis, the blood pressure increased up to 170/110. However, after ultrafiltration dialysis with fluid removal and loss of weight the blood pressure came down to 130/90. Serum renin levels were undetectable 2 and 4 days after nephrectomy. The patient was continued on hemodialysis three times a week and from there on his blood pressure was controlled without requiring medications. Histological examination of the removed kidney showed chronic pyelonephritis, arterial and arteriolar nephrosclerosis without evidence of necrotizing arteriolitis or fibrinoid degeneration.

Discussion

The beneficial effects of lowering the arterial pressure in hypertensive patients with azotemia has been extensively documented (1, 2). Perhaps the main objection to the aggressive management of hypertension associated with renal insufficiency is the further impairment of renal function by decreasing the perfusion pressure and the resultant aggravation of azotemia or uremia. However, Woods and Blythe (3) and Mitchell (4) demonstrated that reduction of arterial pressure in patients with malignant hypertension complicated with azotemia improved the survival rate without deterioration of renal function. Similarly, Mroczek *et al* (5) administered diazoxide intravenously and furosemide orally to 25 patients with severe, drug resistant hypertension complicated with azotemia producing acute repeated reduction of arterial pressure for a 2 week period. By giving this combination the hypertensive disease process was modified and the responsiveness to antihypertensive therapy was reestablished. It follows that aggressive treatment using potent medications is paramount in the control of hypertension with azotemia to prevent further deterioration of renal function and cardiac and cerebral complications. Based on the above studies we proceeded to treat aggressively the patient herein presented. Figure 1 illustrates the blood pressure and course of treatment. None of the antihypertensive medications decreased the blood pressure. However, bilateral nephrectomy produced a prompt and sustained reduction of blood pressure.

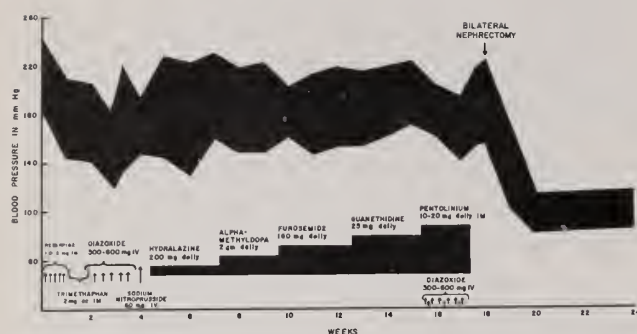


Figure 1

Our previous experience (6, 7) and that of other investigators (8) amply demonstrate resistance to the administration of oral antihypertensive medications in a number of hypertensive patients with end stage renal disease. The patients invariably show an elevated serum renin level and a failure to reduce the blood pressure upon achievement of dry weight (7).

In addition to the above criteria, our patient failed to respond to our most potent parenteral antihypertensive agents such as: trimethaphan, pentolinium, sodium nitroprusside and diazoxide. Hypertension was associated with chronic pyelonephritis and moderately severe arterial and arteriolar nephrosclerosis without fibrinoid degeneration or necrotizing arteriolitis. Thus, parenteral drug resistant "renin dependent" hypertension can be found in patients with end stage renal disease in the absence of renal histological changes pathognomonic of malignant hypertension.

Several investigators have found elevated renin levels in chronic renal disease (7, 8, 9). It is possible that their parenchymal disease has produced the right combination of arterial disease and viable juxtaglomerular apparatus to secrete high amounts of renin which simulates a Goldblatt kidney. This impression is supported by the response of blood pressure to bilateral nephrectomy.

The clinician must be aware that antihypertensive medication may be of no avail in some patients with severe hypertension and azotemia. Our observations suggest that serum renin has a predictive value to screen patients whose hypertension will respond to nephrectomy. Bilateral nephrectomy is the treatment of choice for drug resistant "renin dependent" hypertension in end stage renal disease. The decision to perform surgery rests on the availability of dialysis or renal transplantation to maintain life.

Summary

A severely hypertensive unilaterally nephrectomized patient unresponsive to the use of potent parenteral antihypertensive drugs including long term administration of the experimental drug diazoxide is presented. His hypertension was associated with chronic pyelonephritis and moderately severe arterial and arteriolar nephrosclerosis without fibrinoid degeneration or necrotizing arteriolitis. In addition serum renin levels were consistently elevated. Surgical removal of the remaining kidney produced a prompt and sustained reduction of blood pressure associated with undetectable serum renin levels. During the renoprival state the blood pressure was controlled without requiring antihypertensive agents. Our observations suggest that serum renin has a predictive value in screening patients whose hypertension will respond to nephrectomy. Bilateral nephrectomy is the treatment of choice for drug resistant "renin dependent" hypertension in end stage renal disease.

Resumen

Un paciente severamente hipertenso, con nefrectomía unilateral, no respondió al uso de agentes antihipertensivos potentes. Su hipertensión fue asociada a pielonefritis crónica y nefrosclerosis arterial y arteriolar moderadamente severa sin degeneración fibrinoide o arteriolitis necrotizante. Los niveles de renina en el suero se mantuvieron elevados consistentemente. Al extirpar el riñón restante se produjo un descenso rápido y sostenido de su tensión arterial asociado con una ausencia de niveles de renina circulante. Durante el estado renoprivo la presión arterial fue controlada sin agentes antihipertensivos. Nuestras observaciones sugieren que la detección de niveles de renina en el suero es valiosa para seleccionar qué pacientes hipertensivos con enfermedad crónica renal responderán a nefrectomía. Nefrectomía bilateral es el tratamiento de predilección para hipertensión resistente a drogas y "dependiente de renina" en fallo renal terminal.

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DRAMA EN LA ASAMBLEA

Por: J. Rodríguez Pastor, MD

Una asamblea en la Asociación Médica de Puerto Rico. Habla el Dr. Juan Jíbaro.

DR. JIBARO: *Mister Chairman, I have been discussing for two hours the importance of a new drug in the treatment of that rare African disease of which only five cases have been diagnosed since the times of Hippocrates. I contend that we should make a thorough search for that disease in this island. I further contend.....*

CHAIRMAN: *Let me interrupt you for a minute, doctor. We have here a distinguished guest, an invited lecturer from Europe, who seems to have some difficulty in understanding what you are talking about.*

DR. JIBARO: *Pardon me if I am rude, Mr. Chairman; but we should not invite to our medical meetings lecturers who do not understand our language. A visitor, especially if he is a lecturer, should acquaint himself with the language of the country he is visiting, before he visits that country. If he does not understand us, why did he come? By the way, what kind of a rare language does this distinguished visiting professor speak?*

CHAIRMAN: *Spanish.*

TELON

EDITORIAL

PROGRAMA CONTROL DE ENFERMEDADES VENEREAS: FUNCION Y OBJETIVOS

El Programa Control de Enfermedades Venéreas es una sección adscrita al Programa de Servicios Médico Preventivo. El objetivo principal del programa es el control de la propagación de las enfermedades venéreas en Puerto Rico. La función principal del programa es investigar y examinar todos los casos de sífilis infecciosa y todos los contactos, sospechosos y asociados de estos casos. El objetivo inmediato es reducir la incidencia de todas las etapas de la sífilis al mínimo o erradicarla en su totalidad.

El Programa desempeña seis funciones en el área de las enfermedades venéreas: (1) aplica la epidemiología a todos los casos conocidos de sífilis infecciosa; (2) investiga las serologías reactivas o positivas informadas por laboratorios públicos y privados; (3) promueve las visitas a médicos privados para que éstos informen sus casos al Departamento de Salud y permitan la aplicación de la epidemiología a sus pacientes; (4) promueve así mismo, las visitas a laboratorios públicos y privados; (5) participa en la labor educativa al pueblo sobre estas enfermedades y (6) participa, además, en la investigación y control de casos de sífilis no infecciosa proveyendo tratamiento y seguimiento adecuado a estos pacientes.

Durante el curso de la década de 1960-70 el programa creció gradualmente, desde un pequeño grupo de investigadores hasta su potencial actual que incluye 22 plazas de Técnicos en Epidemiología, 4 Consejeros en Salud Pública y un grupo adecuado de oficinistas. Los puestos están distribuidos a través de toda la isla con una concentración mayor en el área metropolitana.

El programa funciona desde una Oficina Central actualmente ubicada en el Antiguo Hospital de Veteranos, San Patricio. Allí se distribuye el trabajo de toda la isla; a las áreas de: Ponce, Mayagüez, Arecibo, Santurce, Río Piedras, Aguadilla, Caguas, Cataño, Vega Baja y Cauóvanas. Cada una de estas áreas cuenta con personal debidamente adiestrado tanto en los aspectos médicos de las enfermedades venéreas, como en la investigación y localización de casos y posibles casos.

A los efectos de que nuestro programa alcance un grado de excelencia en la realización de su tarea, se hace un llamado a la clase médica para obtener su más decidida cooperación con los técnicos asignados a su área y para que consideren los servicios epidemiológicos como una extensión de su oficina los cuales puedan utilizar tan pronto como se les presente un caso de sífilis infecciosa u otra enfermedad venérea. Trabajando todos en conjunto podremos reducir a un mínimo el impacto en Puerto Rico del resurgimiento casi epidémico de estas enfermedades.

Programa Control de Enfermedades Venéreas

ACTUALIDADES MEDICAS

CRITERIA AND TECHNIQUES FOR THE DIAGNOSIS OF GONORRHEA

.....CRITERIA

Women

Recommended

1. To diagnose gonorrhea in women, culture specimens should be obtained from the cervix and the anal canal and inoculated on separate Thayer-Martin (TM) culture plates or in separate Transgrow bottles. The combination of a positive oxidase reaction of colonies and Gram-negative diplococci grown on either medium provides sufficient criteria for a diagnosis of gonorrhea.
2. For test-of-cure, culture specimens should be obtained from both the cervix and the anal canal, inoculated on either TM or Transgrow medium, and interpreted according to the combination of criteria presented in item 1.

Not Recommended

1. Gram-stained or fluorescent antibody stained smears are not recommended for the diagnosis of gonorrhea in women except as an adjunct to the cultures.
2. The delayed fluorescent antibody technique is not recommended for the diagnosis of gonorrhea.
3. Neither fluorescent antibody stained smears nor the delayed fluorescent antibody procedure is recommended as a test-of-cure in women.

Men

Recommended

1. Microscopic demonstration of Gram-negative, intracellular diplococci on smear of a urethral exudate constitutes sufficient basis for a diagnosis of gonorrhea. Prepare smear by rolling swab on slide; do not rub swab on slide because microscop-

ic morphology will be distorted.

2. When Gram-negative diplococci cannot be identified on direct smear of a urethral exudate, a culture specimen should be obtained from the anterior urethra and inoculated on Thayer-Martin (TM) or Transgrow medium. The combination of a positive oxidase reaction of colonies and Gram-negative diplococci grown on either medium provides sufficient criteria for a diagnosis of gonorrhea.
3. When a test-of-cure or a test for incubating gonorrhea is needed, a culture specimen should be obtained from the anterior urethra and plated on either medium; the culture should be interpreted according to the combination of criteria presented in item 2.
4. In homosexuals, an additional culture specimen should be obtained from the anal canal and pharynx, inoculated on TM or Transgrow medium, and interpreted as in item 2.

Not Recommended

1. Fluorescent antibody staining of smears of urethral exudates is not recommended to diagnose gonorrhea.
2. Fluorescent antibody staining of urethral exudates or the delayed fluorescent antibody procedure should not be used as a test-of-cure.

SPECIAL SITUATIONS

1. In special social, medicolegal, and research situations when specific identification of organisms isolated on either TM or Transgrow medium from the pharyngeal or anogenital region is desired, fermentation reactions should be used to confirm identification of *Neisseria gonorrhoeae*. Fluorescent antibody staining can be used as a confirmatory tool for organisms isolated on either medium if insufficient isolated colonies of suspected gonococci are available for inoculation of fermentation medium or if the organisms

are not longer viable.

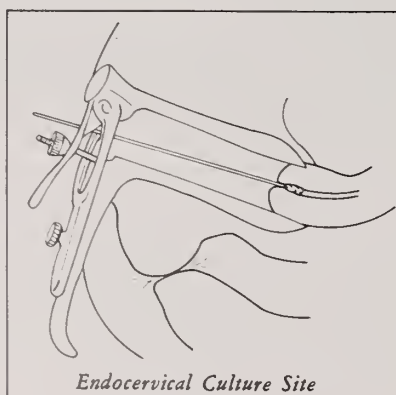
2. Culture on TM medium is the diagnostic procedure of choice in special situations such as suspected gonococcal conjunctivitis, arthritis, or septicemia. Identification of *N. gonorrhoeae* should be confirmed as described in item 1 (Special Situations).
3. Gram staining and fluorescent antibody staining of smears from conjunctivae, joint fluids, or skin lesions can be used as an adjunct in the diagnosis of these manifestations of gonorrhea, particularly when partial therapy may prevent cultural recovery of organisms. (Fluorescent antibody conjugates are check tested for specificity by the Venereal Disease Research Laboratory for use only in a confirmatory test for organisms grown on selective media, and not for staining of direct smears.)

.....TECHNIQUES

I. OBTAIN CULTURE SPECIMEN

Women

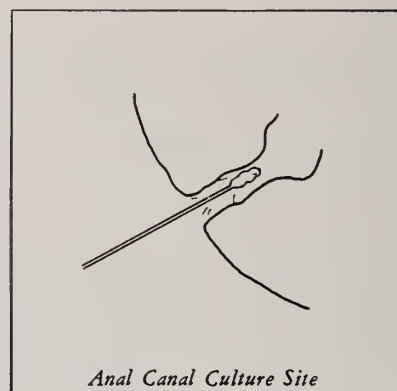
1. **CERVICAL CULTURE** — the best site to culture
 - a. Moisten speculum with warm water; do NOT use any other lubricant.
 - b. Remove cervical mucus, preferably with a cotton ball held in ring forceps.
 - c. Insert clean cotton-tipped swab into endocervical canal; move from side to side; allow several seconds for absorption of organisms to the swab.



2. **ANAL CANAL CULTURE** (also called "rectal culture") — most likely site to be positive when cervix is negative.

Note: This specimen can easily be obtained after the cervical specimen without changing patient's position and without using anoscope.

- a. Insert clean, cotton-tipped swab approximately one inch into the anal canal. (If swab is inadvertently pushed into feces, use another swab to obtain specimen.)
- b. Move swab from side to side in the anal canal to sample crypts; allow several seconds for absorption of organisms to the swab.



3. **URETHRAL or VAGINAL CULTURES** — indicated when the cervical culture is unsatisfactory; e.g., hysterectomy patients and children; or added when maximal sensitivity is desired such as in special social, research, or medicolegal situations.

Urethral

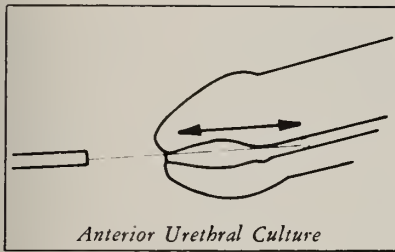
- a. Strip the urethra toward the orifice to express exudate.
- b. Use sterile loop (less painful) or cotton swab to obtain specimen.

Vaginal

- a. Use speculum to obtain specimen from the posterior vaginal vault, or obtain specimen from the vaginal orifice if the hymen is intact.

Men

1. **URETHRAL CULTURE** — indicated when Gram stain of urethral exudate is not positive, in tests-of-cure, or as test for incubating gonorrhea.
 - a. Use sterile bacteriological wire loop to obtain specimen from anterior urethra by gently scraping the mucosa.

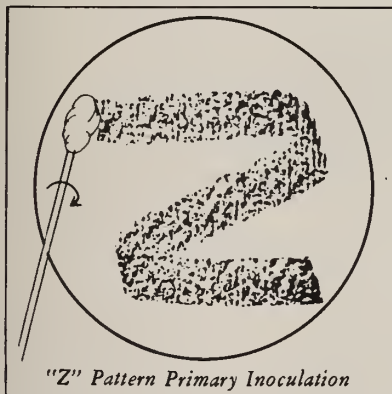


2. ANAL CANAL CULTURE — These can be taken in the same manner as for women.

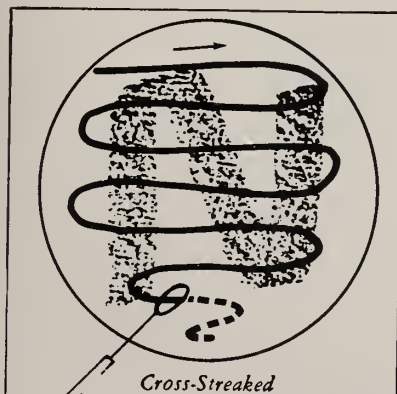
II. INOCULATE THAYER-MARTIN MEDIUM (below) or TRANSGROW MEDIUM

THAYER-MARTIN PLATES

A. Roll swab directly on Thayer-Martin (TM) medium in a large "Z" pattern to provide adequate exposure of swab to plate for transfer of organisms. Less desirable alternative: Place swab in holding medium and refrigerate until plating.



B. Cross-streak immediately with a sterile wire loop, preferably in the clinic. If not done previously, cross-streaking should be done in the laboratory.



C. Place culture in a candle jar as soon as possible.

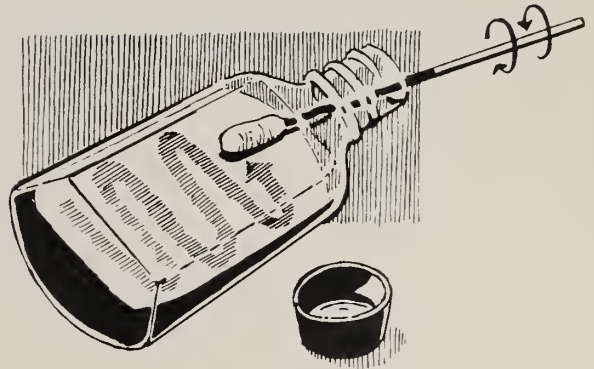
D. Begin incubation of plates the same day.

TRANSGROW BOTTLES

A. Inoculate specimens on the surface of Transgrow medium as follows:

Caution: Keep neck of bottle in elevated position to minimize CO_2 loss.

1. Remove cap of bottle only when ready to inoculate medium.
2. Soak up all excess moisture in bottle with specimen swab and then roll swab from side to side across medium, starting at the bottom of the bottle.



- B. When possible, incubate the Transgrow bottle in an upright position at $35-37^{\circ}\text{C}$ for 16-18 hours before mailing and note this on accompanying request form. Resultant growth survives prolonged transport and is ready for identification upon arrival at the laboratory.
- C. Package the capped Transgrow bottle and request form in a suitable container to prevent breakage and immediately transport to a central bacteriologic laboratory by postal service or other convenient means.
- D. At the laboratory, preincubated Transgrow bottles will be examined immediately for *N. gonorrhoeae*; other bottles will be incubated at $35-37^{\circ}\text{C}$ for 24-48 hours and examined.

Special Considerations.

Preliminary evaluation indicates storage life of Transgrow medium at room temperature maybe in excess of three months.

Many physicians and laboratories are starting to

use this new Transgrow medium; however, some unsatisfactory results may be obtained unless physicians use good techniques in obtaining and inoculating specimens and until the microbiologists become familiar with this new culture procedure; i.e., colony morphology may be atypical on Transgrow medium.

General Considerations

Transgrow, a selective medium for the transport and cultivation of *N. gonorrhoeae*, is used for sending specimens to a central laboratory; on the other hand, TM plates are used when there is immediate access to a laboratory. Transgrow me-

dium under 10 percent CO₂ atmosphere in bottles promotes growth of pathogenic *Neisseria* and suppresses contaminating organisms similarly to Thayer-Martin medium in plates. Transgrow medium maintains viability of pathogenic *Neisseria* for more than 48 hours at room temperature. Validity of culture results depends on proper techniques for obtaining, inoculating, and handling specimens.

(For further information: Center for Disease Control - Attn: Venereal Disease Branch, Atlanta, Georgia 30333 Telephone: 404/633-3311).

RESUMEN DE LAS RECOMENDACIONES DEL COMITÉ ASESOR SOBRE TERAPÉUTICA - CENTRO DE CONTROL DE ENFERMEDADES - ATLANTA, GEORGIA - 25 DE FEBRERO DE 1972

GONORREA CURSO DE TRATAMIENTO RECOMENDADOS PARA INFECCIÓN SIN COMPLICACIONES DE LA FARINGE, CERVIX, URETRA Y RECTO

Droga	Ventajas	Desventajas
INTRAMUSCULAR - Penicilina Procainada Acuosa G-4,8 M. U. con 1.0 gm. de probenecid p.o. (adminis- trarse 30 minutos antes de la inyección, preferiblemente).	Una sola sesión (inyecciones múltiples Detiene la sífilis en incubación.	Sensitividad a la penicilina. Reacciones a la procaina. ¿? Reacciones al probenecid.
ORAL - Ampicilina 3.5 gm. p. o. con 1.0 gm. probenecid p. o. (Pueden ser administradas en forma simultánea).	Una sola sesión - Reacciones inmediatas menos frecuentes.	¿? Aumento en las reacciones de sensitividad. ¿? Reacciones al probenecid. Efectos sobre la sífilis en incubación desconocidos.
PACIENTES EN QUE LA PENICILINA ES CONTRAINDICADA O PACIENTES EN QUIENES LA PENICILINA O AMPICILINA HAN SIDO INEFECTIVAS		
INTRAMUSCULAR - Espectynomicina 2.0 gm. IM en Varones 4.0 gm. IM en Mujeres	Una sola sesión - Toxicidad leve y de corta duración.	Carece de efectividad en contra de la sífilis en incubación.
ORAL - Tetraciclina HCL - 1.5 gm. p.o. en el momento y luego 0.5 gm. p.o. q.i.d. por 4 días (Total 9.5 gm). Otros tipos de tetraciclinas no ofrecen beneficio terapéutico alguno.	Disminuye las tasas de uretritis post-gonocócicas.	Ninguna de las tetraciclinas es efectiva en dosis simples. No es tan efectiva como los cursos anteriores. Requiere buena cooperación del paciente. Efectos sobre la sífilis en incubación desconocidos.

TRATAMIENTO A LOS CONTACTOS

Personas expuestas a casos diagnosticados de gonorrea deben recibir el mismo tipo de tratamiento recomendado para casos de gonorrea.

COMPLICACIONES DE GONORREA

a. Uretritis post-gonocócica - puede ser tratada con tetraciclina 0.5 gm. p.o. qid por lo menos por 7 días.

b. Otras - Aunque el tratamiento para complicaciones severas (gonocócicas, salpingitis, bacteremia, artritis, etc.) debe ser individualizado, dosis masivas repetidas de penicilina acuosa cristalina G han demostrado ser efectivas. La eficacia de cursos de tratamiento a base de antibióticos alternos no ha sido hasta la fecha comprobada.

SEGUIMIENTO

Es aconsejable obtener cultivos uretrales para seguimiento, siete días después de completar el tratamiento en los varones y cultivos cervicales y rectales son aconsejables de 7 a 14 días luego de completar el tratamiento en las mujeres.

SÍFILIS

Todo paciente tratado para gonorrea debe recibir un examen serológico para sífilis. Pacientes que reciben los cursos de tratamiento con penicilina intramuscular recomendados no deben ser sometidos al seguimiento serológico para sífilis. Pacientes tratados con ampicilina, espectynomicina, o tetraciclina deben ser sometidos a seguimiento serológico para sífilis todos los meses por cuatro meses para descubrir una sífilis enmascarada por el tratamiento para gonorrea.

Pacientes con gonorrea y con una sífilis concomitante deben ser sometidos a un curso adicional de tratamiento de acuerdo con la etapa de sífilis.

Mientras las penicilinas de acción prolongada (tales como la Penicilina benzatinica G) son efectivas en la sífiloterapia no hay lugar para estas en el tratamiento de la gonorrea.

----- A N U N C I O

SE ALQUILA

Se alquila oficina para médicos muy cerca del Hospital del Maestro, aproximadamente 300 pies, se incluye teléfono, luz, agua, aire acondicionado, mobiliario de oficina, cortinas. Infórmese llamando al teléfono 766-2250 de 9 a 4 pm, o al 724-1750 fuera de horas laborables.

NOTICIAS

5 de octubre de 1972

El Presidente de la Asociación Médica de Puerto Rico, Dr. Félix S. Vilella Suau, ha autorizado las siguientes declaraciones en torno a las manifestaciones del Ex-Gobernador de Puerto Rico Roberto Sánchez Vilella, sobre la Libre Selección:

"En el Periódico El Mundo, edición del martes 3 de octubre, aparece un reportaje en el que se atribuyen al Ex-Gobernador Roberto Sánchez Vilella, declaraciones en el sentido de que él hizo gestiones durante su incumbencia para que se pospusiera la implementación de la Libre Selección de Médicos para el presente año de 1972.

A tono con estas declaraciones que se le atribuyen a nuestro Ex-Gobernador, deseamos señalar públicamente que el Gobierno de Puerto Rico, a través de su Comisionado Residente, el Lcdo. Santiago Polanco Abreu, solicitó del Congreso de los Estados Unidos el 11 de abril de 1967, la posposición de la Libre Selección, no para 1972 como señala el Sr. Roberto Sánchez Vilella, sino para el 1975, según consta en las actas taquigráficas del Congreso que obran en nuestro poder.

En las declaraciones que se le atribuyen, el Sr. Roberto Sánchez Vilella, señala además que "había mucha reserva por parte de la gente de Gobierno, Presupuesto y el Departamento de Salud, sobre la viabilidad del Proyecto en Puerto Rico". Estamos seguros de que había mucha reserva por parte de la gente del Gobierno, al extremo de que cuando las autoridades federales en el 1967 realizaron una investigación de la aplicación del Título XIX en Puerto Rico, encontraron 16 fallas básicas y solicitaron urgentemente que dichas fallas se corrigieran o de lo contrario Puerto Rico perdería las asignaciones federales.

Si las autoridades de Puerto Rico durante la incumbencia del Ex-Gobernador Sánchez Vilella hubiesen seguido las recomendaciones que una y otra vez les hizo la Asociación Médica, Puerto Rico habría tenido para el 1967 un programa de servicios de salud conforme con lo requerido por el Congreso de los Estados Unidos.

El no aceptarse por parte de las autoridades puertorriqueñas la Libre Selección; el permitir las deficiencias que obligaron el rechazo de 18 hospitales para el Plan Medicare, más la oposición a la ayuda de un seguro de salud para ancianos de 65 años o más, ha costado a la Isla más de \$20 millones de dólares anuales, que en justicia nos correspondía recibir para beneficio de los pobres de Puerto Rico.

La Asociación Médica de Puerto Rico, bueno es repetirlo una vez más, ha tenido siempre un enorme interés en cuanto a la calidad de los servicios que se le brindan a los pacientes médicamente indigentes, actuando siempre de buena fe, y su actual posición tiene el sólo propósito de lograr que el Programa de la Libre Selección comience en bases sólidas, y que a la vez se le

garantice al pueblo de Puerto Rico, al pueblo pobre de Puerto Rico, la mejor calidad de servicios disponibles".

6 de octubre de 1972

En el Periódico El Mundo del martes 3 de octubre aparece un reportaje en el que se atribuyen al Portavoz de la Minoría en la Cámara de Representantes y actual candidato por el Partido Popular Democrático a un escaño en la Legislatura, Dr. Luis Ernesto Ramos Yordán, declaraciones en el sentido de que todo médico responsable de sus deberes con la profesión y la comunidad debe asociarse y respaldar el Programa de la Libre Selección de Médicos, y más adelante señala que la Libre Selección de Médicos es un engaño al público ya que los pacientes no tienen la educación necesaria para escoger al médico que puede curar sus dolencias.

Sin querer entrar en polémicas con el Portavoz del Partido Popular Democrático en la Cámara de Representantes, deseamos responder que no entendemos cómo por un lado se puede respaldar el Programa de la Libre Selección de Médicos y por otro señalar que la Libre Selección es un engaño al público. Nos parece que aquí hay algo que no concuerda.

Sobre que "los pacientes no tienen la educación necesaria para escoger al médico que pueda curar sus dolencias", diferimos del Dr. Ramos Yordán. El pueblo tiene el conocimiento suficiente para diferenciar entre un buen médico y un mal médico. Nuestro pueblo tiene educación necesaria para escoger su médico, y si por alguna razón se equivoca, al tener el derecho de escoger libremente, tiene el derecho de no continuar con ese médico que no llena sus aspiraciones y que no constituye el médico de su fe y de su confianza.

Por otra parte, considera el doctor Ramos Yordán que la Asociación Médica de Puerto Rico ha asumido una posición intransigente que no responde a los postulados y objetivos que exige la medicina y que está exigiendo que se le dé al Programa de Libre Selección todos los fondos que conlleva su implementación total, unos \$180 millones que el Departamento de Salud no tiene disponibles.

Nos extrañan muchísimo estas declaraciones del doctor Ramos Yordán ya que él debe saber que uno de los propósitos de la Asociación Médica de Puerto Rico es el mejoramiento de la salud del pueblo de Puerto Rico y el esclarecer y dirigir la opinión pública en relación con los problemas de la asistencia médica, haciendo que el médico sea de la mayor utilidad para sus pacientes.

Nuestra posición nunca ha sido, ni es, ni será una posición intransigente, sino una sujeta al diálogo sereno y constructivo. Además, no estamos exigiendo los \$180 millones que sabemos que el Departamento de Salud no tiene disponible. Nos parece que el distinguido aspirante a un escaño legislativo no ha entendido la posición de la Asociación Médica de Puerto Rico.

El Portavoz de la Minoría en la Cámara debe tener conocimiento que durante las sesiones legislativas de 1971 y 1972 la Asociación Médica de Puerto Rico presentó a los Presidentes de ambos Cuerpos, legislación para que se investigara la implementación que se estaba haciendo de la Ley 56 de Medicina Integral. ¿Por qué nuestra Hon. Legislatura no respaldó esta legislación o presentó una resolución, para que se investigara la implementación de la Ley 56, tal como lo hiciera la Asociación Médica?

Nuestra posición actual tiene el sólo propósito de lograr que el Programa de Libre Selección comience en bases sólidas y que a la vez se le granticea a los pobres de Puerto Rico servicios de salud de primera calidad, comparables a los que reciben los médicamente solventes.

A continuación reproducimos carta recibida del Dr. Eulogio M. Calderín, de Miami, Florida, quien nos ha pedido la publiquemos para quien le pueda interesar:

"El que estas líneas le escribe es el doctor Eulogio M. Calderín, que tengo el Board de Puerto Rico y que me encuentro acogido al Social Security.

Compañero, mi situación económica dada la poca ascendencia de el retiro es bastante precaria por lo que recurro a usted con el fin de conseguir en su demarcación una suplencia ya que el Social Security me permite ganar hasta dos mil dólares por dos meses o hasta que gane los citados dos mil dólares o en guardias hasta misma cifra.

Cualquier compañero médico que necesite por motivos personales o familiares o por cualquier otra razón que necesite disponer de dos meses yo lo puedo sustituir. Yo he trabajado por espacio de siete años en esa Isla y soy GP.

En espera de su contesta y con el ruego que me perdone es de usted muy respetuosamente,

*Eulogio M. Calderín, MD
2540 S. W. 24 Terrace
Miami, Florida, 33145*

PHYSICIANS RECOGNITION AWARD APPLICANT LIST
FOR 1971 - PUERTO RICO

*Alvarez, Abelardo Ruiz D.
Cuevas Zamora, Rafael
Escalona, Francille M.
Géigel Olivieri, Ana A.
Hernández, Angel W.
Hernández, Genil N.
Isales, Luis M.
Jiménez Vélez, José L.
León Valiente, Ana I.
Marcial, Víctor A.*

*Mayol, Pedro M.
Merille Acosta, José E.
Minino Castillo, S.
Miró Sotomayor, Pedro A.
Montalvo Cordero, José H.
Moreta, Renán A.
Mujica, Juan A.
Namer, José Behar
Pérez Comas, Adolfo
Plaja, Buenaventura
Quiñones Gamboa, Armando
Ramírez Rivera, José
Ramírez Ronda, Carlos H.
Rodríguez Ollerós, Angel
Rodríguez Ernesto R, Jr.
Ruiz Arroyo, Hiram A.
Sierra García, Radamés
Silvestry, Elvin John
Soler Vincenty, Luis E.
Torres Aybar, Francisco G.
Urrutia Carpio, Rubén O.
Vega Vidal, Mercedes
Vergne Marini, Pedro Juan*

FROM HEW NEWS - Oct. 13, 1972

Medicare providers must now file final cost reports with the Social Security Administration within 45 days from the time the provider terminates participation in the Medicare program or undergoes a change in ownership.

The new requirement becomes effective with regulations published in the Federal Register today.

Present Medicare cost reporting regulations are otherwise unchanged. The regulations currently require Medicare providers to submit an annual cost report covering a 12-month operating period. Selection of the period is up to the provider. It need not coincide with any 12-month period the provider has established for other purposes.

The 45-day deadline for filing final cost reports was adopted to protect the Medicare program by requiring the former providers to promptly fulfill their reporting obligations, Robert M. Ball, Commissioner of Social Security, explained.

An earlier proposal - to require that providers' Medicare cost reporting periods coincide with their IRS reporting periods and that they adopt IRS due dates for filing Medicare cost reports - was deleted from the regulations finally approved, Ball said. The Social Security Administration did not desire to burden providers with reporting requirements that might, in some instances, increase operating expenses. The deletion also took into consideration the fact that most participating providers that can do so effectively, already use the same reporting year for both Medicare and IRS.

They're debating your future in Washington right now. Who's standing up for you?

National health insurance is the issue, and the way you'll practice in the future is at stake. One proposal would federalize the entire medical system.

Who's standing up for your rights? Contrary to what you may think, the AMA.

We've testified repeatedly against a government controlled medical system. Even before it was proposed, the AMA had introduced its own program of voluntary national health insurance called "Medicredit." And we've pushed for it hard. To date, the AMA has enlisted 167 members of Congress as its co-sponsors — more than can be claimed for any other national health insurance bill.

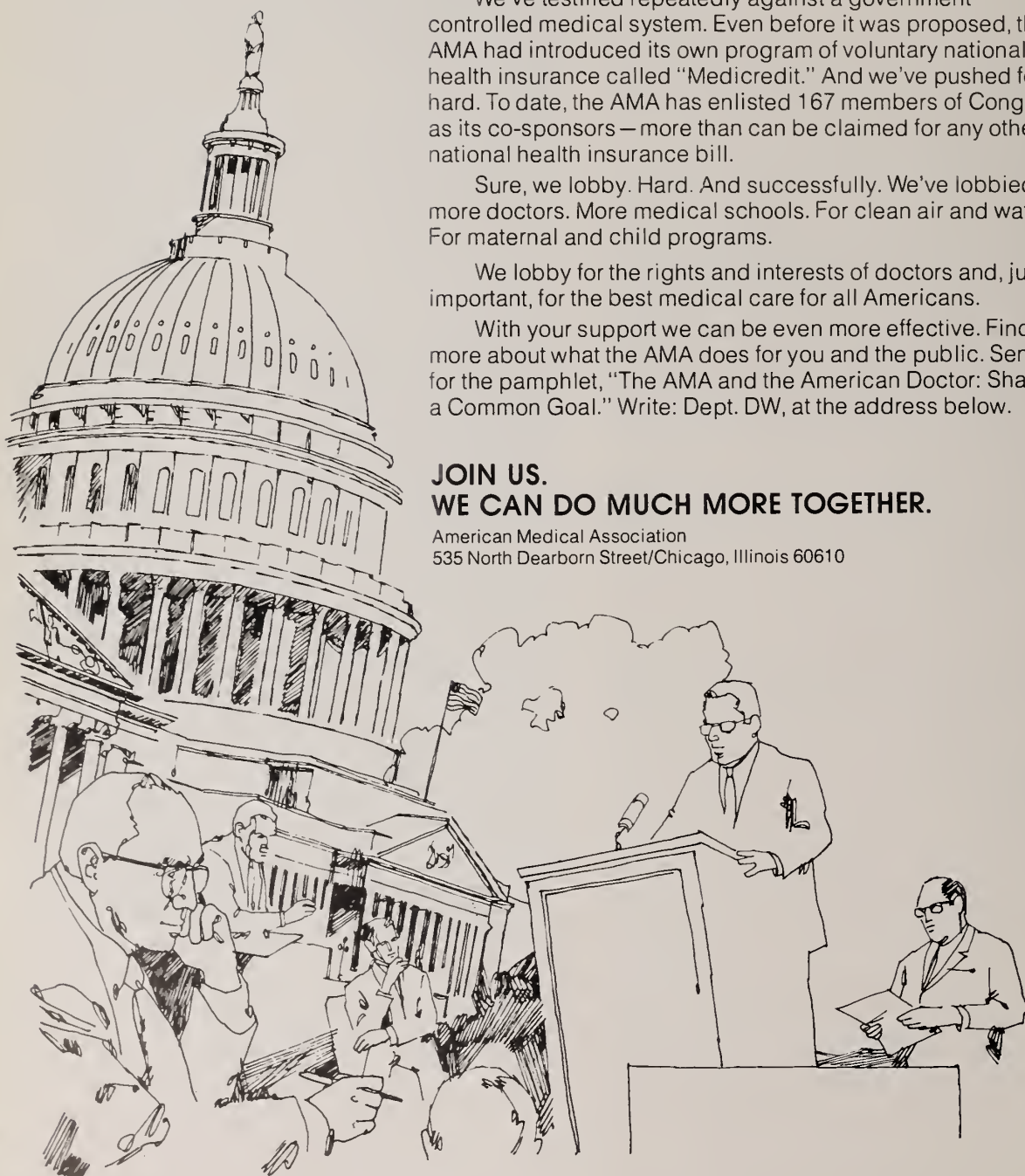
Sure, we lobby. Hard. And successfully. We've lobbied for more doctors. More medical schools. For clean air and water. For maternal and child programs.

We lobby for the rights and interests of doctors and, just as important, for the best medical care for all Americans.

With your support we can be even more effective. Find out more about what the AMA does for you and the public. Send for the pamphlet, "The AMA and the American Doctor: Sharing a Common Goal." Write: Dept. DW, at the address below.

**JOIN US.
WE CAN DO MUCH MORE TOGETHER.**

American Medical Association
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Maalox[®]-protected aspirin



Reduces the risk of gastric distress from aspirin, especially when high doses are used, as in arthritis. And Ascriptin[®] is advertised only to you...not to your patient.

WILLIAM H. RORER, INC. Fort Washington, Pa. 19034





Methionine supplementation enhances protein efficiency.

Neo-Mull-Soy contains no corn sugars.

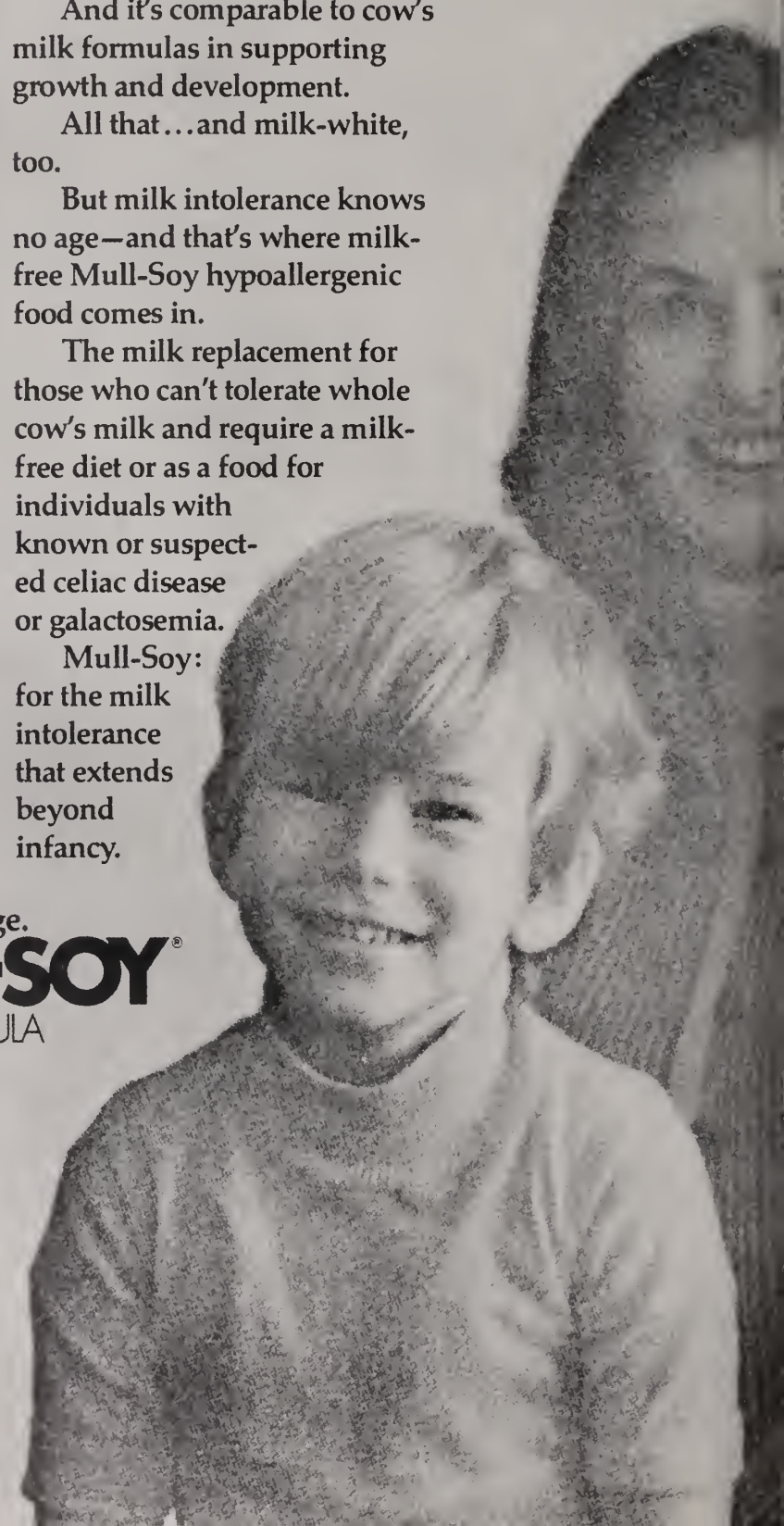
And it's comparable to cow's milk formulas in supporting growth and development.

All that...and milk-white, too.

But milk intolerance knows no age—and that's where milk-free Mull-Soy hypoallergenic food comes in.

The milk replacement for those who can't tolerate whole cow's milk and require a milk-free diet or as a food for individuals with known or suspected celiac disease or galactosemia.

Mull-Soy: for the milk intolerance that extends beyond infancy.



Milk intolerance knows no age.

No need to compromise when you specify Neo-Mull-Soy or Mull-Soy. They meet the needs of milk intolerant patients of all ages.

Neo-Mull-Soy milk-free formula is designed as a replacement diet for the infant under a year old who may manifest symptoms of milk intolerance—diarrhea, colic, vomiting, rhinorrhea, anorexia, eczema.

Its protein, fat, and carbohydrate levels approximate those of human milk.

For infants under one year of age.

NEO-MULL-SOY®

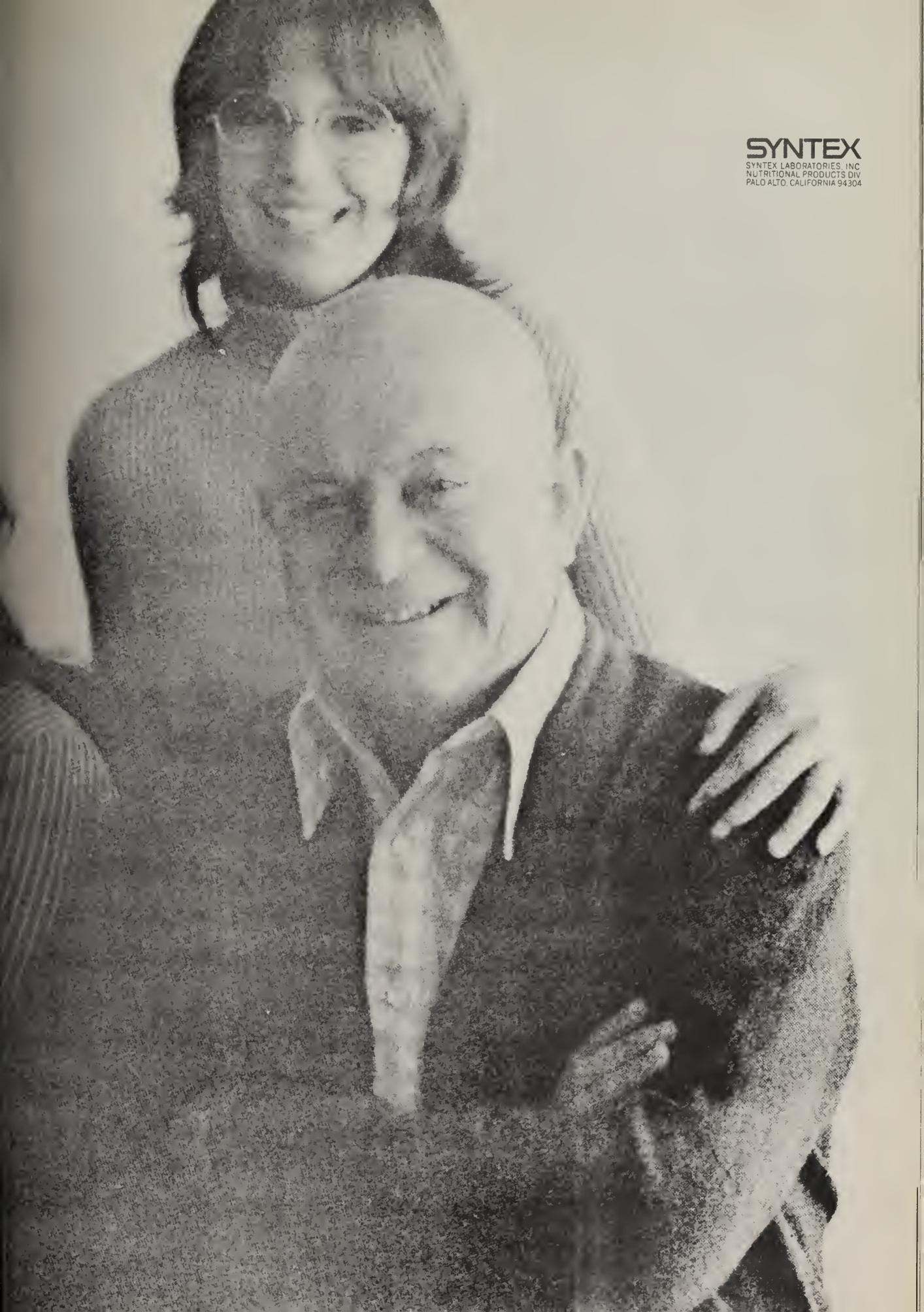
SOY PROTEIN ISOLATE FORMULA

For children and adults.

MULL-SOY®

SOY FORMULA

SYNTEX
SYNTEX LABORATORIES, INC.
NUTRITIONAL PRODUCTS DIV.
PALO ALTO, CALIFORNIA 94304



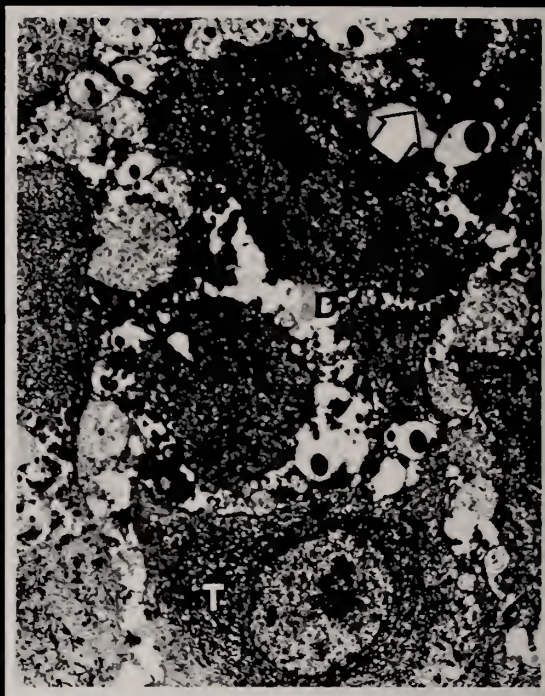
Efudex[®] (fluorouracil) works where it counts...*



Lesion #2—Two days after initiation of therapy. Electron micrograph of solar keratotic skin from patient's hand.

Typical abnormalities are:

Malpighian cells [containing an abundance of thick tonofibrils (T)] which are connected with well-developed desmosomes (D). Note the clumped tonofibrils in the so-called 'dyskeratotic' cell (arrow) indicative of solar keratosis. No change can be noted at this level after two days of therapy. $\times 5000$ (12/16/71)



Lesion #3—Two weeks after initiation of therapy. Electron micrograph of skin from patient's hand.

Improvement shown:

Less conspicuous desmosomes (D), widened intercellular spaces and Malpighian cells showing a remarkable reduction of tonofibrils (T). The arrow indicates a degenerating dyskeratotic cell. $\times 5000$ (12/31/71)

Solar, actinic or senile keratoses

By whatever name they may be known, they commonly occur as multiple lesions and chiefly on the exposed portions of the skin. Because they may be premalignant, it is generally agreed that they should be treated. Surgery, cryotherapy, or electrodesiccation may present certain drawbacks, both for the physician and the patient, but there is Efudex[®] (fluorouracil)—as an alternative to conventional therapy.

Sequence of therapy— Selectivity of response

The easily applied Efudex cream or solution usually begins to show effects within a few days—an erythema in the area of the lesions. Within two weeks after initiation of therapy, this reaction usually reaches its height of unsightliness and discomfort, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

Acceptable results

Treatment with Efudex (fluorouracil) provides highly acceptable cosmetic results posttherapeutically. The incidence of scarring is low.* This is particularly important with multiple facial lesions. Efudex should be applied with care near the nose, eyes and mouth.

5% cream/solution—a Roche exclusive

Only Roche formulates the 5% cream and solution—high in patient acceptability—economical—and high in clinical efficacy than the 2% formulation for lesions of the hands and forearms.

*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

In treating solar keratoses which may be premalignant.



Before treatment—12/14/71



After treatment—Two weeks after
therapy stopped—1/28/72

This patient's solar keratoses
responded to
Efudex (fluorouracil) 5%

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Use with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation, burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—inflammation, stomatitis, suppuration, scaling, swelling, irritability, metallic taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover affected area twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 5% or 5% fluorouracil on a weight/weight basis, combined with propylene glycol, tris(hydroxymethyl)ammonium chloride, hydroxypropyl cellulose, parabens (methyl and

propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

An alternative to
conventional therapy

Efudex[®]
(fluorouracil)
cream/solution



**Not too little, not too much...
but just right!**

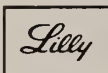
"Just right" amounts of Ilosone Liquid 250
can be dispensed easily from the pint bottle in any quantity
you specify to meet your patients' precise needs—
without regard to package size.

ready-mixed
Ilosone® Liquid 250

Erythromycin Estolate

(equivalent to 250 mg. of base per 5-ml. teaspoonful)

*Additional information available
to the profession on request.
Eli Lilly and Company
Indianapolis, Indiana 46206*



100204

Carnation Evaporated Milk. Baby's first taste of real food.

Nothing artificial. It's a real food. With naturally occurring protein and all other nutrients intact. Add supplementary vitamins and carbohydrate and it's a complete, nourishing diet that doesn't pretend to be anything but good, honest nutrition babies thrive on.



For natural formulas

With the means at hand to drastically reduce the number of deaths each year from uterine cancer, we have embarked on a nationwide, life-saving program. Its goal is a Pap test by 1976 for every woman 20 years or older to whom the test is applicable, and for younger women at risk. An ambitious program, doctor, and one which can only be realized with your help.

We are faced with these facts: only 53% of women over

20 have ever had a Pap test; only 20% get a Pap test periodically; each year about 43,000 new cases are diagnosed; this year 12,000 women in this country will die of uterine cancer. And about 75% of these deaths will result from cervical cancer—as you know, almost 100% curable when diagnosed early and treated promptly.

We hope to reach women in the target group not only with the message about the *vital*

Pap test, but also with the urgency of including it in the *regular* health checkup. The mortality rate from uterine cancer could thus be dramatically curtailed.

Clearly action is called for. Coordinated action—involving the doctor, the patient, the American Cancer Society—a partnership for life.

a partnership for life



American Cancer Society



Cuando comen lo que les gusta
y no lo que deben...



ayude a cubrir "el déficit" de vitaminas con

Unicap Therapeutic

10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
Vitamina D	10 mcg.
Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

Upjohn

PR 5226.1 MAY, 1969
6811 MARCA REGISTRADA EN E.U.A.: UNICAP THERAPEUTIC
UPJOHN INTER-AMERICAN CORPORATION / CAPARRA / PUERTO NUEVO

Librium® and (chlordiazepoxide HCl) concomitant use

Librium (chlordiazepoxide HCl) is used as adjunctive antianxiety therapy concomitantly with certain specific medications of other classes of drugs, such as cardiac glycosides, anti-hypertensive agents, diuretics, anticholinergics and antacids.

Antianxiety effectiveness: Demonstrated in a broad range of psychologic and physical dysfunctions; indicated when reassurance and counseling

are not enough and until, in the physician's judgment, anxiety has been reduced to tolerable appropriate levels.

Effect on mental acuity: Usually minimal on proper maintenance dosage.

Safety: An excellent clinical record. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated.

**in relief of clinically
significant anxiety**

Librium®
(chlordiazepoxide HCl)
5-mg, 10-mg, 25-mg capsules
up to 100 mg daily in
severe anxiety

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debili-

tated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the

elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation; extrapyramidal symptoms, increased decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110



BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

HISTOPLASMOSIS AGUDA - EPIDEMIA EN SAN GERMAN 291

Rafael Díaz Martínez, MD, MPH, FCCP

GENTAMICIN: A CLINICAL STUDY 295

Roberto F. Fortuño, MD, FACS and Rubén Cartagena, MD

FIEBRE REUMATICA ACTIVA SIMULANDO APENDICITIS AGUDA 298

Rafael Villavicencio, MD, Jorge Sánchez, MD y Amalia Martínez Picó, MD

DIHYDROGENATED ALKALOIDS OF ERGOT IN GERIATRIC PATIENTS:
SYMPTOMATIC TREATMENT OF CEREBROVASCULAR INSUFFICIENCY ... 301

C. Kaye, MD, MPH

SECCION DE LIBROS 304

NOTICIAS 305

THE FRANCIS A. COLLETT WAY
LIBRARY OF MEDICINE
BOSTON

10 JAN 1973

The negative power of clinically significant anxiety
in angina pectoris...

This man feels he is living
on borrowed time.

During anginal attacks, patients may suffer intense apprehension. More frequently, however, they experience a continuing sense of less severe but nonetheless disproportionate anxiety.

Reduction of such clinically significant anxiety is important, since undue emotional stress may precipitate further anginal episodes.

Adjunctive Librium (chlordiazepoxide HCl) may be especially suitable for relief of clinically significant anxiety and emotional tension in anginal patients because of its generally prompt therapeutic effectiveness and wide margin of safety. In a recent double-blind randomized study, Librium (chlordiazepoxide HCl) was administered for relief of moderate anxiety in 20 anginal patients seen in office practice over a 20-week period. Symptoms of emotional distress related to anxiety were rated at base-line, one week, two weeks and monthly thereafter. Relief was obtained notably early in therapy. The clinical results demonstrated that Librium offers the coronary patient an antianxiety drug that, in the author's opinion, is both effective and safe. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated. (See summary of prescribing information.)*

Librium (chlordiazepoxide HCl) is used concomitantly with certain specific medications of other classes of drugs, such as cardiac glycosides, diuretics and antihypertensive agents, whenever anxiety is clinically significant. The drug should be discontinued after anxiety has been reduced to appropriate levels.

The positive power of
adjunctive
Librium®
(chlordiazepoxide HCl)
10-mg, 25-mg capsules
up to 100 mg daily
for moderate
to severe anxiety
accompanying angina pectoris

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

*Levine, S.: "Angina Pectoris and Emotional Overlay," Scientific Exhibit presented at the Annual Meeting of the Maine Medical Association, Kennebunkport, Me., June 13-15, 1971.

A copy of the Levine study may be obtained from your Roche representative.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

the uncover girl...



Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

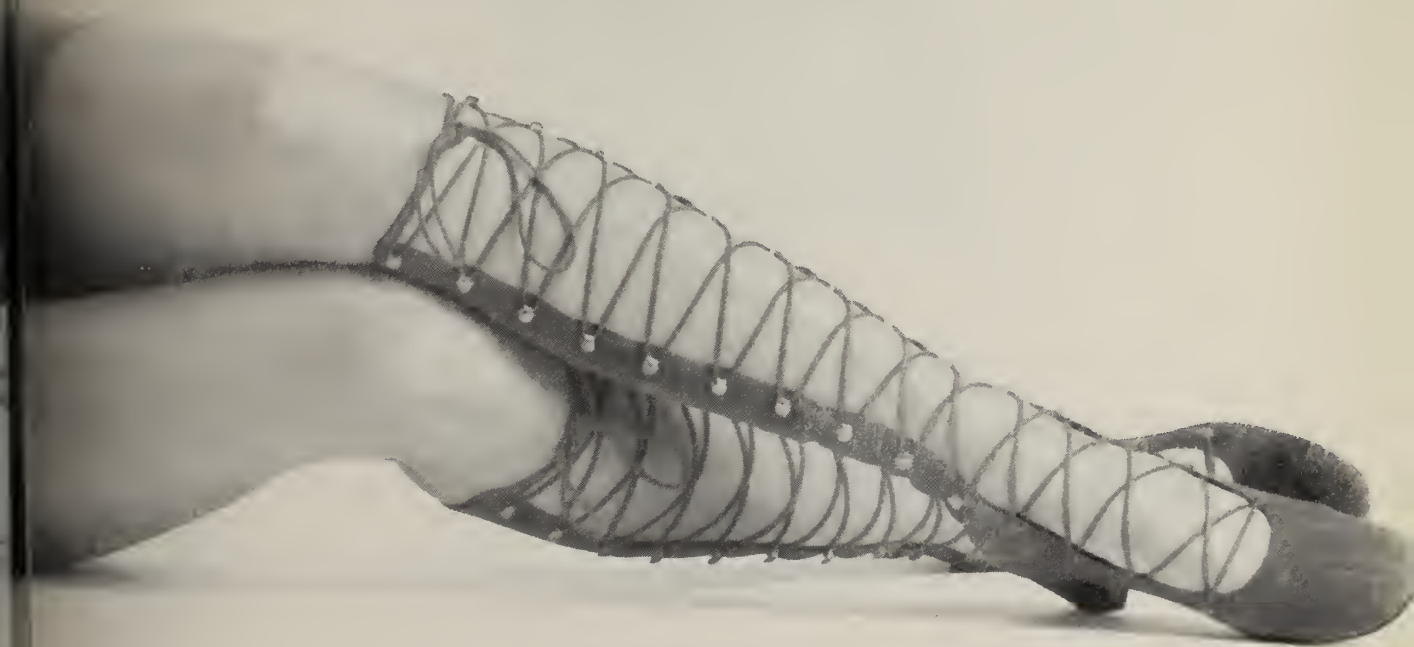
If used under occlusive dressings or for a prolonged period, watch for

Her contact dermatitis* cleared smoothly by **Vioform®-Hydrocortisone** (iodochlorhydroxyquin and hydrocortisone)

Nothing defeats today's abbreviated clothing styles like an exposed skin disorder. That's why physicians and patients have come to depend on the multiple benefits of Vioform-Hydrocortisone. Because it combines the antibacterial, antifungal actions of Vioform with the anti-inflammatory and antipruritic actions of hydrocortisone, Vioform-Hydrocortisone can prove effective in so many common skin disorders—where topical steroids alone can't cope with frequently coexisting bacterial or fungal infection.

antifungal • antibacterial • anti-inflammatory • antipruritic

*This drug has been evaluated as possibly effective for this indication. See brief prescribing information.



sis of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after continuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Reports include: Hypersensitivity, local burning, irritation, pruritus. Continue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

USAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl

sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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C I B A

BOLETIN

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Fundado en 1903

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Anuncios y Suscripciones:

El Boletín se publica mensualmente. Todo material de anuncio está sujeto a aprobación por la Junta Editora.

Reimpresos:

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

Second Class postage paid at San Juan, Puerto Rico.

Why send him to the islets of Langerhans?



Since sulfonylureas promote the release of insulin which is lipogenic and helps transport glucose into adipose tissue...

And since many overweight patients already have normal or high levels of endogenous insulin, why not consider DBI-TD?

It lowers blood sugar without stimulating

insulin secretion from the pancreas. And this may be important to the dieting diabetic.

In adult-onset, nonketotic diabetics uncontrolled by diet alone...

DBI-TD[®] Geigy
phenformin HCl

lowers blood sugar without raising blood insulin.

DBI[®] phenformin HCl
Tablets of 25 mg.

DBI-TD[®] phenformin HCl
Timed-Disintegration
Capsules of 50 and 100 mg.

Indications: Stable adult diabetes mellitus; sulfonylurea failures, primary and secondary; adjunct to insulin therapy of unstable diabetes mellitus.

Contraindications: Diabetes mellitus that can be regulated by diet alone; juvenile diabetes mellitus that is uncomplicated and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); during or immediately after surgery where insulin is indispensable; severe hepatic disease; renal disease with uremia; cardiovascular collapse (shock); after disease states associated with hypoxemia.

Warnings: Use during pregnancy is to be avoided.

Precautions: 1. *Starvation Ketosis:* This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria which, in spite of relatively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.**

2. *Lactic Acidosis:* This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic

determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.

3. *Hypoglycemia:* Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin.

Adverse Reactions: Principally

gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake. (B) 98-146-103-D (6/72)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of
CIBA-GEIGY Corporation
Ardley, New York 10502

With the means at hand to drastically reduce the number of deaths each year from uterine cancer, we have embarked on a nationwide, life-saving program. Its goal is a Pap test by 1976 for every woman 20 years or older to whom the test is applicable, and for younger women at risk. An ambitious program, doctor, and one which can only be realized with your help.

We are faced with these facts: only 53% of women over

20 have ever had a Pap test; only 20% get a Pap test periodically; each year about 43,000 new cases are diagnosed; this year 12,000 women in this country will die of uterine cancer. And about 75% of these deaths will result from cervical cancer — as you know, almost 100% curable when diagnosed early and treated promptly.

We hope to reach women in the target group not only with the message about the *vital*

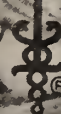
Pap test, but also with the urgency of including it in the regular health checkup. The mortality rate from uterine cancer could thus be dramatically curtailed.

Clearly action is called for. Coordinated action — involving the doctor, the patient, the American Cancer Society — a partnership for life.

a partnership for life



American Cancer Society



an antacid
in good taste



Camalox™ Tablets are a new taste experience. Their refreshing vanilla-mint flavor provides high patient appeal, an important consideration in antacid therapy. A unique Rorer process* not only assures exceptional flavor, it also provides a tablet that is soft to chew, not brittle, flaky, nor does it leave a gritty aftertaste.

A balanced formulation of magnesium and aluminum hydroxides with calcium carbonate, Camalox Tablets have proved superior to other leading ethical antacids in critical *in vitro* tests. They neutralize more acid, act faster, and last longer. Non-constipating, Camalox Tablets are designed for long-term therapy and for

quick relief during peak distress periods of hyperacidity.

Taste Camalox Tablets—a flavorful way to deliver a high level of antacid activity.

COMPOSITION: Balanced formulation of magnesium and aluminum hydroxides with calcium carbonate.

INDICATIONS: As an antacid in the treatment and management of peptic ulcer, gastritis, gastric hyperacidity, hiatal hernia, peptic esophagitis, heartburn, indigestion and upset stomach.

WARNING: Camalox should not be used in patients who are severely debilitated or suffering from kidney failure.

SUPPLIED: Camalox Tablets—bottles of 50 tablets and boxes of 100 tablets (in foil strips).

Camalox Suspension—white liquid in 16 oz. (pint) bottle.

CamaloxTM

VANILLA-MINT TABLETS

for the acute distress of hyperacidity

WILLIAM H. RORER, INC.



Fort Washington, Pa. 19034

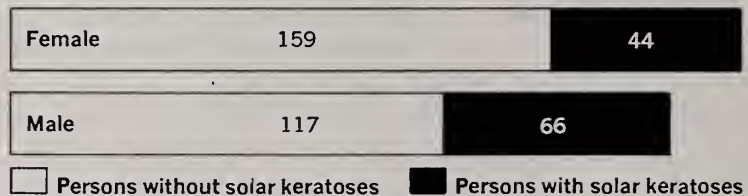
What it means to live and work in Tipton County, Tennessee

**Persons who are white and
over 40 have one chance in four
of having solar keratoses...
which may be premalignant**

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

**Prevalence of solar keratoses in white persons
over 40 in Tipton County, Tennessee**



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Solar, actinic, senile keratoses

Called by many names, the typical lesion is flat or slightly elevated, brownish or reddish in color, papular, dry, adherent, rough, sharply defined; usually multiple lesions, chiefly on exposed portions of the skin.

Sequence/selectivity of response

Erythema in areas of lesions may begin after several days of therapy; height of reaction (only in affected areas)* usually occurs within two weeks, declining after discontinuation of therapy. Since this response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

Cosmetic results

Cosmetic results are highly favorable. Incidence of scarring is low—important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

5% cream—a Roche exclusive

Only Roche formulates the 5% cream... high in patient acceptability... high in clinical efficacy, especially for lesions of hands and forearms... economical.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

an alternative to conventional therapy **Efudex[®]** (fluorouracil) cream/solution



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110



It's about time somebody told the true story of the American Doctor.

You'd agree 100% on that. There have been too many of the other kind of story.

You know that the vast majority of American doctors are honest, hardworking, skilled and dedicated human beings who have the interests of their patients at heart.

That's exactly what the AMA is trying to make the public aware of.

One of the many ways the AMA is doing it is through its special communications program.

Perhaps you've seen pages in newspapers and national magazines signed "America's Doctors of Medicine." They're part of this program. It tells the true story of what it takes to become a doctor. The ways American medicine has improved the public's health. And to express the profession's concern about health by providing information which will help every American lead a healthier life.

We're telling this story for you, the American doctor. If we are to continue to represent you effectively, we need your support.

Find out more about what the AMA does for you and the public. Send for the pamphlet, "The AMA and the American Doctor: Sharing a Common Goal." Write: Dept. DW, at the address below.

JOIN US.

WE CAN DO MUCH MORE TOGETHER.

American Medical Association
535 North Dearborn Street/Chicago, Illinois 60610



HERE

Fractures



Wherever it hurts,
Empirin Compound with
Codeine usually provides
the relief needed.

HERE

Bursitis



In general, only pain so severe
that it requires morphine is
beyond the scope of
Empirin Compound with Codeine.

prescribing convenience:
up to 5 refills in 6 months,
at your discretion (unless
restricted by state law); by
telephone order in many states.

Empirin Compound with
Codeine **No. 3**, codeine
phosphate* 32.4 mg. (gr. ½);
No. 4, codeine phosphate*
64.8 mg. (gr. 1). *Warning—
may be habit-forming. Each
tablet also contains: aspirin
gr. 3½, phenacetin gr. 2½,
codeine gr. ½.

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

WHEREVER IT HURTS



Low back pain
HERE

EMPIRIN[®] COMPOUND c CODEINE

#3, codeine phosphate* (32.4 mg.) gr. ½
#4, codeine phosphate* (64.8 mg.) gr. 1



Break the ulcer circuit to hyperacidity, hypermotility and ulcer pain.

Pro-Banthine[®] propantheline bromide A Relief Factor in Peptic Ulcer



Worry, frustration, job pressure—all set up excessive vagal currents in patients with peptic ulcer.

Pro-Banthine "insulates" the stomach, the duodenum and the lower intestinal tract—the sites where these destructive currents take their toll.

This "insulation" helps block excessive enteric activity and acidity, thus helping to provide the proper environment for the healing of peptic ulcers.

It's nice to know that Pro-Banthine provides this protection at a dosage that causes little or no discomfort and that, unlike ataractic agents, Pro-Banthine does not cloud the patient's awareness or thought processes.

By moderating excessive vagal currents Pro-Banthine relieves spasm, acid burn and pain. By reducing gastric motility Pro-Banthine also prolongs the activity of antacids.

Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

In theory a curare-like action may occur, with possible loss of voluntary muscle control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males

with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

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HISTOPLASMOSIS AGUDA EPIDEMIA EN SAN GERMAN

Rafael Díaz Martínez, MD, MPH, FCCP

Ocho jóvenes varones, cuyas edades fluctúan entre 12 a 26 años de edad, residentes del Bo. Rosario de San Germán, entraron en las Cuevas del Peñón del barrio mencionado, adquiriendo histoplasmosis. Sólo se mostró clínicamente un caso serio que hubo necesidad de tratar con Amphotericin B. Las Cuevas del Peñón son de difícil acceso y, quizás por este hecho, no tenemos el sexo femenino en este grupo de enfermos.

Distribución Geográfica

Los estudios realizados por varios médicos puertorriqueños como son los doctores Suárez, Torres de Blasini, Sifonte, De Jesús, Figueras y otros, han mostrado la existencia de la histoplasmosis en Puerto Rico y, al recopilar los datos, podemos apreciar que esta micosis es más frecuente en las zonas alejadas de las costas. En Estados Unidos, los sitios endémicos son el Valle Missisipy en las ciudades de Missouri, Arkansas, Tennesse y Kentucky (sin negar la existencia de la enfermedad en otras ciudades).

En Puerto Rico, los sitios donde han sido informados los casos de histoplasmosis siguen el mismo patrón. Las incidencias más altas con pruebas de histoplasminas (sol. 1:100) por el Departamento de Salud Federal en 1955 en niños de 1er. grado en la Isla, fueron Naranjito con 59.5 por ciento, Caguas 45.8 por ciento, San Sebastián 25.6 por ciento, Vega Baja 22.6 por ciento y Mayagüez en dos Escuelas Rurales 70.6 por ciento (1). El primer caso de histoplasmosis es informado en 1960 por la Dra. Torres de Blasini y sus colaboradores, en un paciente de Gurabo (1). Tres años más tarde, el Dr. Manuel De Jesús y compañeros informan el primer caso de histoplasmosis sistémica en una niña de tres años de Caguas (2). En 1966, los doctores Torres de Blasini y Carrasco Canales hacen estudios del suelo

en Puerto Rico y se encuentra el histoplasma capsulatum en las Cuevas de Utuado y Aguas Buenas (3). Dr. Sifontes y compañeros en 1964 informan un brote de histoplasmosis en excursionistas a las Cuevas de Aguas Buenas (4). En 1968, los doctores Luis G. De Jesús y F. Ramos Morales informan tres nuevos casos de esta micosis pulmonar en las Cuevas de Aguas Buenas (5). Nos ocupa en este trabajo un brote de histoplasmosis en San Germán. (Véase fig. 1).

Etiología

El agente etiológico de esta enfermedad es el histoplasma capsulatum, organismo que habita en el suelo y que llega a los pulmones en forma de esporas inhaladas al respirar un ambiente contaminado. Parasita primeramente el sistema retículo endotelial y rara vez se encuentra extra celular. Los individuos afectados por esta micosis presentan un cuadro clínico parecido a un estado gripal agudo, (aproximadamente en el 25 por ciento de los casos) que en la mayoría de las veces evoluciona favorablemente sin tratamiento específico.

Materiales y Método

En marzo 1971, se efectuó una clínica en el Centro Antituberculoso de San Germán. En ella, presentaron un joven de 14 años de edad, quien hacía un mes estaba padeciendo de tos fuerte, con expectoración amarillenta, dolor en el pecho, fiebre alta, escalofríos y cansancio. Recibió tratamiento antigripal, con lo que mejoraron ligeramente los síntomas, pero continuó con marcado cansancio, palidez, episodios de tos y fiebre. Una radiografía del tórax mostró un moteado exudativo en ambos campos pulmonares. Este caso fue necesario ingresarlo y tratarlo con Amphotericin B. El historial reveló que una semana antes de enfermarse el joven había entrado junto a otros compañeros a las Cuevas del Peñón. Todos habían tenido los mismos síntomas, pero él era el único que continuaba enfermo. Se procedió a una investigación, encontrándose que todos los demás tenían síntomas similares, y las pruebas cutáneas, serológicas y radiografías fueron positivas a histoplasmosis (Véase tablas).

Estudios radiográficos mostraron moteado exudativo disminuidos en ambos campos pulmonares (Fig. 2). Un caso presentó imágenes de nódulos hiliares.

Del Departamento de Salud, Centro Médico, Mayagüez, Puerto Rico. Presentado en la Convención Anual de la Sociedad Médica Distrito Occidental, el 14 de enero de 1972.

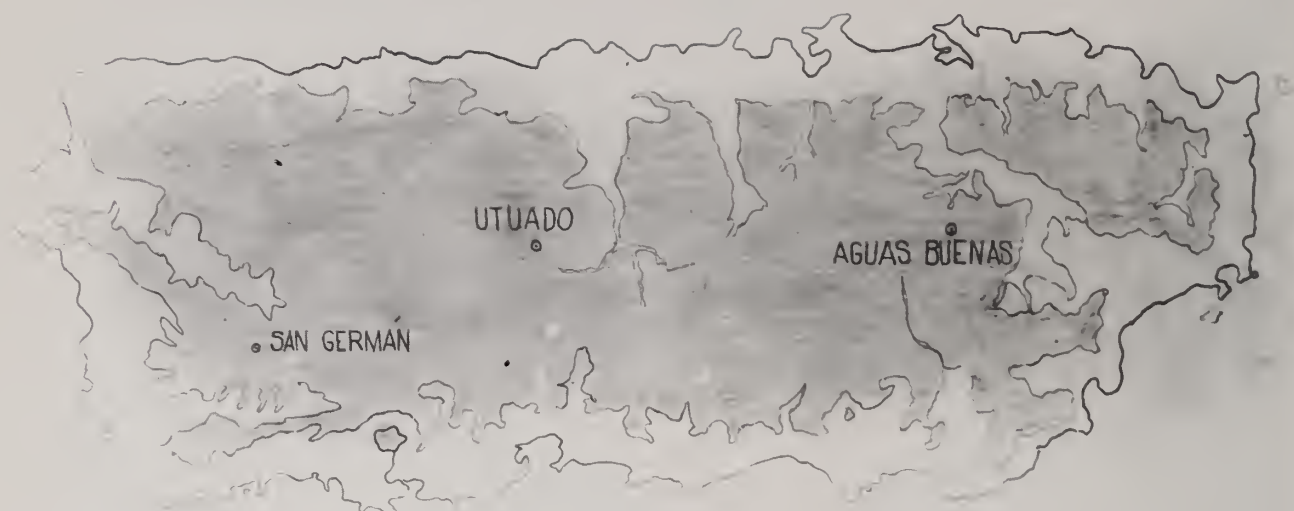


Figura número 1.

TABLA I: SINTOMATOLOGIA

Síntomas	Casos
a) Dolor en el cuerpo	5
b) Cefalalgia	7
c) Fiebre y escalofríos	5
d) Cansancio	7
e) Pérdida de peso	4
f) Tos seca	4
g) Mareos	2
h) Tos con expectoración	2

TABLA II: PRUEBAS INTRACUTANEAS

Histoplasmina en MM.	Tuberculina en MM. PPDS.
10	Negativos
6	"
7	"
2	"
10	"
5	"
10	"
7	"

Discusión

El hallazgo de estos casos de histoplasmosis, es una prueba más de la existencia de esta micosis en Puerto Rico. Su distribución geográfica es más frecuente en las zonas centrales, donde existen condiciones favorables climatológicas y de los suelos, que contienen sustancias como las excretas de las aves ("birds dropping") y del murciélago ("bat guano") que favorecen el crecimiento del hongo. El *histoplasma capsulatum* es favorecido en su crecimiento por sustancias como los carbohidratos y nitrógenos que están en gran concentración en las excretas de estos animales. La sintomatología de los casos es parecida al cuadro gripal. Las pruebas intracutáneas de *histoplasma* fueron todas positivas, excepto en el caso núm. 4, que midió 2 mms., y ya que todos los demás hallazgos fueron positivos, quizás hubo un error en la lectura. Las pruebas de tuberculinas fueron todas negativas.

En las pruebas de complemento, ocho fueron positivas al antígeno de *histoplasmina* y fase de levadura, con siete casos de reacción cruzada con *blastomicosis* y dos con *coccidioidomicosis*. El estudio radiográfico del tórax de siete casos mostró imágenes de moteado exudativo en ambos campos pulmonares y uno mostró lesiones en los hilios. A todos los casos, se le hizo lavado bronquial para investigar hongos con resultados negativos. Se tomaron muestras del suelo y se enviaron al

TABLA III: PRUEBAS SEROLOGICAS - FIJACION DE COMPLEMENTO

Caso	Edad	Histoplasmosis	Blastomycosis		Coccidioidomycosis
		Histoplasmina	Levadura	Levadura	Coccidiolina
1	26	1:128	1:32	1:32	0
2	14	1:128	1:32	1:64	1:8
3	15	1:8	1:32	1:132	0
4	14	1:16	1:32	1:64	1:8
5	13	1:8	0	0	0
6	16	1:64	1:128	1:64	0
7	12	1:32	1:32	1:64	0
8	14	1:16	1:256	1:64	0



Figura número 2.

Departamento Micología del Colegio Agricultura y Artes Mecánicas, sin poder aislar el histoplasma capsulatum. El diagnóstico diferencial de esta enfermedad es la tuberculosis, bronconeumonía, sarcoidosis, neoplasma y enfermedades ocupacionales. Se basa el diagnóstico en el historial, pruebas cutáneas, pruebas serológicas, hallazgos radiológicos y, sobre todo, en el hallazgo del hongo, bien sea en los tejidos o secreciones del paciente o en el suelo donde se adquirió la enfermedad.

Conclusiones

El hallazgo de ocho casos de histoplasmosis en ex-

cursionistas a las Cuevas del Peñón en el Bo. Rosario de San Germán, se suma a aquellos en las Cuevas de Aguas Buenas y a las de Utuado. Teniendo Puerto Rico una topografía con montañas bajas y en muchas de ellas, siendo abundante la existencia de cuevas, es de alertar a los Médicos y Autoridades de Salud Pública, el que se esté consciente de este nuevo hallazgo y pensar que son numerosas las otras fuentes de esta infección que deben existir en la Isla.

No se debe subestimar los resultados de infección por este hongo, que puede variar desde asintomático hasta una condición sistémica con resultados fatales para el enfermo. Esta micosis causa manifestaciones radiográficas que pueden mal interpretarse y tratarse por tuberculosis, (como hasta ahora seguramente se está haciendo), por lo que recomendamos establecer en Puerto Rico, el hacer pruebas cutáneas de histoplasmina a todos los casos sospechosos de tuberculosis. Debe divulgarse el peligro de adquirir la enfermedad al explorar cuevas sin protección adecuada.

Resumen

Se informan ocho casos de histoplasmosis pulmonar en jóvenes varones excursionistas quienes entraron a las Cuevas del Bo. Rosario de San Germán, Puerto Rico. La distribución geográfica, los hallazgos clínicos y radiográficos son discutidos. Se hacen recomendaciones con respecto a establecerse la prueba histoplasmina en todo caso sospechoso de tuberculosis.

A nuestro entender, esta es la epidemia con mayor número de casos informados en Puerto Rico.

Summary

Eight cases of pulmonary histoplasmosis are reported

in young men who explored a cave in Barrio Rosario, San Germán, Puerto Rico. This is the largest epidemic traced to a single site reported from Puerto Rico. The clinical and radiological findings of the cases are discussed and the geographic distribution and ecology of *Histoplasma Capsulatum* are reviewed. Suspected cases of pulmonary tuberculosis in areas where histoplasmosis is endemic should be tested with histoplasmin as well as tuberculin.

Reconocimiento

El autor agradece la cooperación de la Dra. Angelita Ramírez Irizarry, Presidente Comité Científico Soc. Médica Distrito Oeste, Dr. Luis Roure, Micólogo C.A.A.M. y grupo técnicos epidemiólogos del Control TB en la Región Oeste.

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NOTA DEL EDITOR

Es sumamente importante obtener la muestra de sangre para estudios serológicos de diagnóstico en infecciones micóticas antes de aplicar la prueba intradermal, por razones obvias que se olvidan.

GENTAMICIN: A CLINICAL STUDY

Roberto F. Fortuño, MD, FACS
Rubén Cartagena, MD

Gentamicin is a broad-spectrum antibiotic complex derived from *Micromonospora purpurea* (1). The antibiotic was first studied by Weinstein and co-workers in 1963 (2). It was isolated, purified and characterized by Rosselot and others in 1964 (3). Recently this antibiotic complex has been shown to consist of three components designated as C1, C2 and C1A with molecular weights of 477, 463 and 449 respectively (4). The gross structural formula has been proposed by Cooper as shown in Figure 1 (4).

Gentamicins are classified as aminoglycosides, compounds in which a sugar containing an amino group is attached via glycosidic linkage to some other fragment. Other antibiotics in this group include streptomycin, kanamycin and neomycin.

The mechanism of action of gentamicin as well as other aminoglycosides is by inhibition of protein syntheses by misreading at the ribosome level. The degree of misreading is dose-related and its lethal action inhibited by chloroamphenicol and augmented by puromycin (5).

The objective of this study is to assess the effectiveness and safety of gentamicin in the management of selected urinary infections of gram negative bacillary etiology.

Materials and Methods

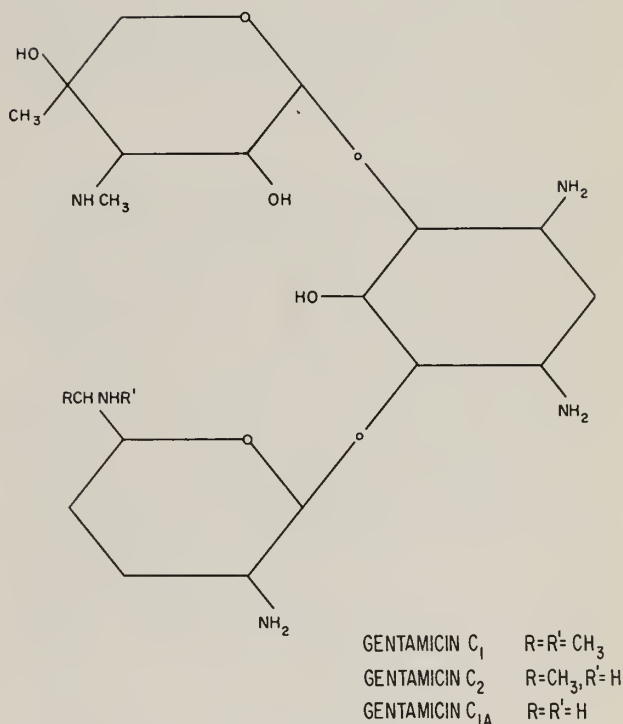
Twenty-five patients were selected from the Puerto Rico Medical Center and admitted to the Department of Urology of San Juan Municipal Hospital from September 1970 to May 1971. These patients had known urinary tract infections caused by gram-negative bacteria proven by urine cultures. There were 13 males and 12 females varying in age from 15 to 67 years, the duration of infection ranged from several weeks to fifteen years. These patients were treated with gentamicin as the only chemotherapeutic agent. Surgical interventions were performed

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This study was supported in part by a grant from Schering Corporation.

FIG. 1

GENTAMICIN C COMPONENTS



when indicated. The drug was administered intramuscularly in a dose of 1.5 mg. per kilogram of body weight per day in three divided doses. The duration of therapy was ten days; except in two cases in which the drug was discontinued due to adverse reactions. Urine cultures were taken prior to initiation of therapy and at seventy-two hour intervals during and after therapy.

Renal function was monitored by serial determinations of B.U.N., creatinine, creatinine clearance and urinalysis. SGOT and CBC were also done three times a week. All subjects were carefully observed for auditory and vestibular dysfunction, but no routine audiometry or caloric tests were performed. Results of treatment were evaluated on clinical and bacteriological bases. Two months after completion of therapy the patients were re-evaluated.

Results

In Table I the causative organisms are presented. Two thirds of our patients were infected with a single organism, while the rest showed mixed infections. *Proteus*, *klebsiella* and *pseudomonas* predominated. Pure *E. coli* infections appeared in only 16 percent.

The complicating factors which helped to perpetuate infection in our patients are described in Table II. In 88 percent the cases at least one of these complicating factors were present. Complete resolution of signs and symptoms was observed in 64 percent upon completion of therapy. Some degree of improvement was noticed in another 24 percent (Table III). One of our patients failed to show any improvement with therapy, while in two the drug had to be discontinued due to adverse reactions.

The bacteriological response, as determined by urine culture performed following treatment, is described in Table IV. Elimination or marked reduction of organisms occurred in 28 percent of the cases. In the rest the causative organism persisted or a new infection appeared.

Therapy had to be discontinued in two of our patients. A young man with a history of schistosomiasis, developed marked elevation of SGOT, SGPT and serum bilirubin, accompanied by pain and tenderness over the hepatic area. One month after completion of therapy he was completely asymptomatic. In the other one, therapy was discontinued when she developed a severe rash soon after initiation of therapy. Other patients showed some laboratory abnormalities during therapy as described in Table V.

Discussion

Gentamicin is a relatively new antibiotic which has been used in the treatment of gram-negative infections. Its effectiveness in urinary tract sepsis has been proven in other studies. Cox obtained a bacteriological cure of 71 percent in his study of patients with urosepsis (6).

In our study the bacteriological response may be considered poor. In 64 percent of the patients we were not able to permanently sterilize the urine with our treatment. We wish to emphasize that this study deals with severe chronic infection in patients with permanently damaged urinary tracts. This is illustrated in Table I, which shows a high incidence of resistant bacteria. *E. coli* appears in only 37 percent of our patients, while in ordinary urinary infections, the incidence of this bacteria is over 80 percent. The

TABLE I: CAUSATIVE ORGANISMS

A. Simple Infections:	
1. <i>Proteus</i>	20 percent
2. <i>E. Coli</i>	16 percent
3. <i>Klebsiella</i>	16 percent
4. <i>Pseudomonas</i>	12 percent
5. <i>Aerobacter</i>	4 percent
	68 percent
B. Mixed Infections:	
1. <i>E. Coli</i> & <i>Enterococci</i>	8 percent
2. <i>E. Coli</i> & <i>Proteus</i>	4 percent
3. <i>Pseudomonas</i> & <i>Proteus</i>	4 percent
4. <i>Pseudomonas</i> & <i>Enterococci</i>	4 percent
5. <i>Klebsiella</i> & <i>Proteus</i>	4 percent
6. <i>E. Coli</i> & <i>Pseudomonas</i>	4 percent
7. <i>Klebsiella</i> & <i>Enterococci</i>	4 percent
	32 percent

TABLE II: COMPLICATING CONDITIONS

1. Lithiasis	5
2. B. P. H.	4
3. Neurogenic Bladder	2
4. Urethral Stricture	2
5. Vesico Ureteral Reflux	2
6. Diabetes Mellitus	2
7. Urethral Valves	1
8. Renal Tuberculosis	1
9. Ca of Bladder	1
10. Urethral Diverticuli	1
11. Papillary Necrosis	1

TABLE III: CLINICAL RESPONSE

1. Complete Resolution of Signs and Symptoms	64 percent
2. Marked Improvement	4 percent
3. Moderate Improvement	12 percent
4. Slight Improvement	8 percent
5. Indeterminate	8 percent
6. Failure	4 percent

TABLE IV: BACTERIOLOGICAL RESPONSE

1. Elimination of Causative Organisms	24 percent
2. Marked Reduction of Causative Organisms	4 percent
3. Elimination of Causative Organism With Superinfection	16 percent
4. Resistance of Causative Organisms	28 percent
5. Resistance of Causative Organism with Superinfection	16 percent
6. Indeterminate	12 percent

TABLE V: LABORATORY ABNORMALITIES DURING THERAPY

1. Increase in Serum Creatinine	68 percent
2. Increase in B U N	40 percent
3. Decrease in Creatinine Clearance	28 percent
4. Transient Elevation of S.G.O.T.	8 percent
5. Marked Elevation of S.G.O.T.	4 percent

clinical response however, is more encouraging since sixty-eight percent of our cases were rendered asymptomatic upon initiation of therapy. In 80 percent, the clinical improvement was accompanied by a temporary but favorable bacteriological response. These findings lead us to recommend the use of this drug for the management of acute exacerbations of chronic urinary tract infections.

In general the drug was well tolerated. The only serious reaction appeared in young man who developed laboratory evidence of hepato-toxicity. It should be stated that he probably had pre-existing liver disease secondary to schistosomiasis. Perhaps this patient should not have been selected for the study.

Regarding renal function, the decrease in creatinine clearance is not impressive, specially once the absolute values are examined. In none of the cases it was a reason for discontinuation of therapy. This decrease in renal function was slight in the majority of the cases it returned to normal in the immediate follow-up period. BUN and creatinine elevations occurred in a higher percentage of the cases and it is of interest to notice that in many of the patients in whom BUN and creatinine increased, the creatinine clearance remained unchanged. It is suggested that these laboratory changes may be caused by extrarenal factors, such as increased protein catabolism and not to the nephrotoxic action of gentamicin itself.

Vestibular and auditory dysfunction has been reported with gentamicin therapy (7). None of our patients showed clinical evidence of this complication. But perhaps some auditory or vestibular dysfunction would

have been detected had audiometry and caloric tests been performed in all the cases.

The absence of hematological toxicity is consistent with other studies (8).

Summary

We have analyzed the clinical findings and laboratory studies in twenty-five patients treated with gentamicin. Complete resolution of signs and symptoms occurred in 64 percent of the cases. A favorable bacteriological response was obtained in 28 percent of the cases. Most of the patients tolerated the drug well.

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FIEBRE REUMÁTICA ACTIVA SIMULANDO APENDICITIS AGUDA

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Jorge Sánchez, MD

Amalia Martínez Picó, MD

El dolor abdominal como una de las manifestaciones clínicas de la fiebre reumática aguda se viene mencionando en varios textos y publicaciones desde hace más de un siglo (1). A pesar de ello no se reconoce su importancia como un síntoma del proceso reumático agudo excepto cuando viene acompañado de alguno de los criterios de Jones (2).

El propósito de este artículo es discutir un caso de fiebre reumática activa que se presentó con un cuadro de abdomen agudo. Con ello intentamos enfatizar el valor diagnóstico de este síntoma, así como la importancia de la fiebre reumática dentro del diagnóstico diferencial de la apendicitis aguda.

Resumen Clínico

Paciente de 11 años de edad que se presenta con la queja principal de dolor abdominal, malestar general, náuseas y vómitos intermitentes de cinco días de duración. El día de su llegada a la sala de emergencia se le añade al cuadro: fiebre (38°C), localización del dolor en el cuadrante inferior derecho del abdomen, y artralgias.

El examen físico reveló un paciente bien desarrollado, bien nutrido, febril y agudamente enfermo. La exploración de oídos, nariz y garganta era normal y los pulmones estaban claros. El examen del corazón reveló solamente taquicardia (120/min.), los tonos cardíacos eran normales, y no se detectó soplo cardíaco. En la exploración del abdomen el cirujano describe dolor a la palpación profunda en el punto de McBurney, sin signo de rebote ni defensa abdominal. El tacto rectal fue positivo, con dolor marcado en la exploración de la fosa ilíaca derecha. No se describen hallazgos positivos en las extremidades. El hemograma reveló una hemoglobina de 9.9 gm. y un conteo de leucocitos de $9,100/\text{mm}^3$ con 90 por ciento de segmentados y 10 por ciento de linfocitos. El análisis de orina fue normal y la radiografía de abdomen negativa.

Se hizo el diagnóstico de apendicitis aguda y se le practicó una apendectomía. El apéndice se describió como normal tanto macroscópica como microscópicamente. El paciente toleró el acto quirúrgico bien, y no hubo complicaciones postoperatorias inmediatas.

Curso Clínico

En el primer día de período post-operatorio la fiebre y el dolor abdominal persistían. El dolor articular se hizo más intenso, la rodilla izquierda estaba dolorosa, enrojecida y caliente. El tobillo izquierdo también estaba doloroso y caliente. Al día siguiente, a la auscultación cardíaca se apreció taquicardia con disminución de los tonos cardíacos. El S_1 estaba marcadamente disminuido, el S_2 estaba normal y apareció un S_3 en el apex. Se auscultó un soplo holosistólico grado 3/6 en foco mitral con transmisión a la axila y región escapular izquierda, y otro mesodiastólico de frecuencia baja, grado 1/4 en la punta (soplo de Carey-Coombs).

El electrocardiograma reveló un intervalo PR de 0.20 segundos, compatible con un bloqueo de primer grado (fig. 1). Las radiografías de torax y articulaciones fueron normales. Se le ordenó un nuevo hemograma así como pruebas de actividad con los siguientes resultados: Hb 9.9 gm.; 18,000 leucocitos $/\text{mm}^3$ con 85 por ciento de segmentados y 15 por ciento de linfocitos. La velocidad de sedimentación globular fue de 60 mm/hr, proteína C-reactiva 8+ y títulos de antiestreptolisina 0 de 500 unidades Todd.

Al ser evaluado el caso por el Cardiólogo Pediatra se hizo el diagnóstico de fiebre reumática activa con insuficiencia mitral, e inmediatamente se comenzó el tratamiento con penicilina procaínica y prednisona a base de 1 mg./lb. por 24 horas en dosis divididas.

La respuesta clínica fue dramática, pues 36 horas más tarde el paciente ya estaba asintomático. A los siete días de haber comenzado el tratamiento ya las pruebas de actividad estaban dentro de los límites normales (Tabla I) y se comenzó la disminución gradual de prednisona hasta discontinuarse por completo.

Al cabo de un mes de comenzado el tratamiento el paciente fue trasladado a un hogar de convalecencia, y aún estaba presente el soplo de insuficiencia mitral. Un año más tarde su auscultación cardíaca era normal.

Actualmente este paciente lleva a cabo sin restricción alguna todas las actividades propias de su edad y continúa con su profilaxis de penicilina benzatínica G

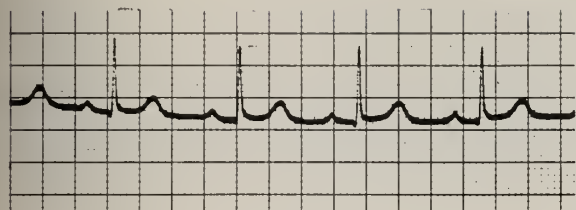


Fig. 1: Derivación II del caso reportado. Se aprecia una frecuencia cardíaca de 80/min. con un intervalo PR de 0.20 seg.

TABLA I

	VSG	PCR	TASO
2-5-71	60 mm./hr.	+ 8	500 U.T.
* 2-8-71	63 " "	+ 6	625 " "
2-15-71	11 " "	NEG.	625 " "
2-21-71	8 " "	NEG.	333 " "
3-1-71	8 " "	NEG.	250 " "

* Comienza de terapia con penicilina procaina y prednisona.

por vía intramuscular cada 28 días.

Comentarios

Este caso ilustra claramente la confusión diagnóstica que puede ocasionar la presencia de dolor abdominal en un paciente con fiebre reumática activa. En el caso presentado el dolor abdominal fue intenso y persistente, precediendo a la poliartritis migratoria y a la carditis, los dos criterios mayores presentes en él. Este dolor no logró ser atribuido a ninguna otra causa que no fuese el propio proceso reumático en actividad.

Creemos importante el mencionar que en nuestro caso la cirugía no ocasionó efecto adverso alguno tanto en la carditis como en la evolución del proceso reumático activo. Esta experiencia ha sido compartida por el grupo del King's County Hospital en Nueva York en su serie de pacientes con fiebre reumática activa simulando apendicitis aguda. La morbilidad y mortalidad de la apendicitis aguda tampoco se altera por la presencia del proceso reumático (3).

El dolor abdominal que acompaña el cuadro de fiebre

reumática ha sido descrito como uno de comienzo insidioso, de distribución difusa, y rara vez localizado. Su duración suele ser de dos a tres días y por lo regular precede a las otras manifestaciones reumáticas (4). La explicación exacta para este dolor abdominal en el proceso reumático se desconoce aún (5). En ciertas ocasiones se ha localizado en el cuadrante superior derecho debido a congestión hepática aguda como consecuencia de carditis aguda y fallo congestivo.

La incidencia de este dolor abdominal se ha informado como variable, desde un 5 a un 20 por ciento (1, 3, 6). En el estudio más reciente, de 199 niños con fiebre reumática, a 5 de ellos (2.5 por ciento) se les practicó una apendectomía antes de hacerse el diagnóstico de fiebre reumática (3).

En la sección de Cardiología Pediátrica del Hospital Universitario se han revisado todos los expedientes de los 150 pacientes con fiebre reumática, siendo el paciente reportado el único con estos hallazgos. Al revisar todas las apendectomías en nuestro hospital en los últimos cinco años no se encontraron casos similares. Este caso aislado da a nuestra institución una incidencia de 0.66 por ciento.

Debemos efectuar en todo paciente con posible apendicitis una auscultación cuidadosa antes de proceder con la cirugía, para detectar la presencia de alguno o todos los siguientes signos de carditis:

- 1) disminución de los tonos cardíacos, especialmente el primer sonido.
- 2) aparición de un tercer sonido.
- 3) soplos:
 - a) holosistólico y de alta tonalidad en foco mitral con propagación a la axila izquierda y espalda (insuficiencia mitral)
 - b) mesodiastólico, de baja tonalidad, en punta (Carey-Coombs); generalmente difícil de auscultar debido a su escasa intensidad.

A esto debe seguir un examen cuidadoso de las articulaciones en busca de signos indicativos de poliartritis.

Además contamos con pruebas de laboratorio sencillas que pueden ser de gran utilidad en nuestro diagnóstico diferencial (Tabla II). Estas pruebas nos ofrecen una evidencia objetiva aunque no específica de la presencia de un proceso reumático inflamatorio alguno.

Creemos que se debe considerar siempre la fiebre reumática dentro del diagnóstico diferencial de la apendicitis aguda. Ambas tienen su mayor incidencia en niños de 5 a 12 años y como vemos ambas pueden presentarse de modo muy similar.

Es obvio que al confirmarse la etiología reumática del dolor abdominal le evitaremos al paciente el tener que sufrir una laparotomía. Sin embargo estamos de

TABLA II

	FIEBRE REUMÁTICA	APENDICITIS AGUDA
ELECTROCARDIOGRAMA	BLOQUEO DE PRIMER GRADO	NORMAL
VELOCIDAD DE SEDIMENTACIÓN GLOBULAR	MARCADAMENTE ELEVADA	NORMAL O DISCRETAMENTE ELEVADA
TÍTULO DE ANTISTREPTOLISINA O	ELEVADO (> 333 U.T.).	NORMAL (< 333 U.T.)
PROTEÍNA C-REACTIVA	POSITIVA	NEGATIVA

acuerdo en aconsejar el acto quirúrgico cuando persista una duda auténtica en el diagnóstico de apendicitis aguda. Creemos que es preferible realizar la apendectomía en presencia de fiebre reumática activa antes de exponernos a las graves consecuencias de un apéndice perforado.

Resumen

Al discutir el cuadro clínico de un paciente con fiebre reumática activa simulando una apendicitis aguda se enfatiza:

- 1) la presencia de este síntoma como parte del cuadro de la fiebre reumática.
- 2) la evaluación preoperatoria que debe hacerse en todo paciente de apendicitis aguda donde haya duda sobre la posibilidad de una fiebre reumática.
- 3) en caso de que persista alguna duda en el diagnóstico no debe vacilarse en llevar a cabo la operación.

Summary

A case of a patient with acute rheumatic fever si-

mulating acute appendicitis is reported. Emphasis is made on:

- 1) the frequency with which abdominal pain accompanies an active rheumatic process.
- 2) adequate pre-operative evaluation for patients with abdominal pain in whom the possibility of rheumatic fever has to be ruled out.
- 3) an unhesitant surgical approach if any reasonable doubt persists.

Reconocimiento

Reiteramos nuestro agradecimiento a la Sra. Norma C. González por su valiosa asistencia en la elaboración de este artículo.

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DIHYDROGENATED ALKALOIDS OF ERGOT IN GERIATRIC PATIENTS: SYMPTOMATIC TMENT OF CEREBROVASCULAR INSUFFICIENCY

C. Kaye, MD, MPH

What can the general physician do for "old people" - specifically those who have difficulty with the ordinary function of day-to-day living, such as walking, eating, bathing, and dressing? How can the physician most effectively manage patients who suffer confusion, memory losses, disorientation, depressive mood, the symptoms of mental decline often associated with "old age"?

Cerebrovascular insufficiency (CVI) has been frequently considered the source of such symptoms. When this is the case, improvements in cerebral circulation - specifically blood flow, vascular resistance, oxygen utilization - should alleviate the patient's symptoms and complaints. Such beneficial effects on cerebral circulation have been observed in pharmacologic investigations (1-3) with dihydrogenated alkaloids of ergot*. Furthermore, the results of clinical studies (4-6) in geriatric patients have shown improvement in a range of symptoms characteristic of CVI. Gerin (4), for example, saw better performance of daily-living activities and relief of many physical complaints in his patients, while Triboletti and Ferri (5) observed improved attitude and mood in their patients. Ditch, Kelly and Resnick (6) found the most impressive effects of the treatment with dihydrogenated alkaloids of ergot (1) to be an improvement of cognitive and intellectual capacities, in addition to beneficial changes in their attitude and mood, performance of basic self-care tasks, and certain physical manifestations.

Together these studies demonstrate that this drug can improve a wide range of disconcerting and often incapacitating symptoms associated with aging and generally attributed to CVI. In implementing a comprehensive therapeutic program for older age patients,

we are constantly alert and ready to evaluate new treatment regimens that show promise for the improvement of functionality and unmanageability of geriatric patients. Therefore, we chose to validate— by our own experience — the reported usefulness of the dihydrogenated alkaloids of ergot in geriatric patients suffering from symptoms related to CVI.

Material and Method

We examined 50 institutionalized patients to determine whether they could be admitted to the study. All participants were required to be at least 65 years old, and have, in addition to other symptoms representative of CVI, at least two of the following key manifestations: confusion, deviation from normal mood (e.g., depression), impairment of recent memory and/or mental alertness. Patients were excluded from the trial for any circumstance that might interfere with their reasonable participation or with scheduled assessments. For example, patients with psychosis, posttraumatic brain damage, postinfective brain disease, cerebral neoplasm, or marked deterioration were excluded. Patients were also excluded if they were experiencing an emotional upset (e.g., the illness of a spouse) or a ward transfer. Finally, no patient who had taken psychoactive drugs, vasodilators, or sedatives on a regular basis during the preceding three weeks were admitted to the study. Of the 50 patients screened, 33 (20 men and 13 women) met the criteria of the protocol and were included in the study.

All patients were given 2 tablets of the dihydrogenated alkaloids of ergot sublingually three times a day (3 mg daily), before or after meals, for 12 weeks. Concomitant administration of medication necessary to treat concurrent medical ailments (e.g., digitalis) was permitted on a regular basis, provided such medication was not expected to modify the actions and effects of the study drug. Other medications, such as sedatives and antidepressants were allowed, but only on an occasional basis; prolonged use of such agents disqualified the patient from further participation in the study.

The efficacy of the treatment was determined by assessments of change observed in 17 preselected manifestations of CVI. We also recorded an "overall impression" of therapeutic effect. This was not derived from the individual items on the checklist, but rather from a judgment of the patient's total status. These assessments were rated from normal (1) to markedly abnormal (7) before the study to establish a baseline, and every three weeks thereafter for 12 weeks. At each three-week interval after the trial began, the phy-

* - Dihydrogenated alkaloids of ergot, Hydergine^R, Sandoz Pharmaceuticals.

TABLE I: MEAN IMPROVEMENT OF CVI MANIFESTATIONS: PRETREATMENT VS. WEEK 12

Item	Mean Pretreatment	Mean Week 12	Mean Improvement ¹
<u>More Incapaciting/Predominant Symptomatology</u>			
Confusion	4.93	4.33	0.60***
Mental Alertness	4.54	3.96	0.58***
Motivation - Initiative	4.62	4.28	0.34**
Memory	5.19	4.59	0.60***
Indifference to Surroundings	4.31	3.93	0.38**
Unsociability	4.10	3.59	0.51***
Uncooperativeness	4.32	3.93	0.39*
<u>Less Severe/Frequent Symptomatology</u>			
Bothersome	2.44	2.39	0.05
Mood - Depression	2.70	2.48	0.22*
Irritability (cantankerousness)	2.76	2.80	-0.04
Emotional Lability	2.81	2.81	0.0
Fatigue	2.46	2.54	-0.08
Self Care	3.64	3.40	0.24
Appetite (Anorexia)	2.23	2.08	0.15
Dizziness	3.11	2.11	1.00***
Nocturnal Cramps	3.67	2.56	1.11**
Paresthesias	3.00	2.27	0.73**
Overall Impression of Patient	4.38	3.90	0.48***

¹Negative score indicates worsening.

***p < .01

**p < .05

*p < .10

sician also made a global evaluation of each patient's general progress. This global was designed to rate changes ranging from very much improved (+3) through no change (0) to very much worse (-3).

The Student t-test⁷ was used to determine the significance of the change that occurred in each item from baseline to week 12. Only data obtained from those patients who were symptomatic pretrial were analyzed.

The effect of the drug on blood pressure was determined also, from measurements made before the study and at 3, 6, 9, and 12 weeks of treatment.

Results

Of the 33 participants in the study, 29 completed the full course of treatment with dihydrogenated alkaloids of ergot, 17 men and 12 women (mean age, 74 years). Four patients were disqualified because they failed to meet the requirements of the protocol; one refused medication, one was transferred to another hospital, a third had a history strongly suggestive of psychosis, and the fourth received a psychoactive agent immediately before the study.

Analysis of data pertaining to the 17 checklist symptoms and the "overall impression" (Table I) showed that, on average, many items were improved significantly by the end of the 12-week study. The improvements of greatest clinical, as well as statistical, significance were those obtained in seven symptoms of psychologic and social disturbances. These had been both the most frequent and most incapacitating symptoms seen in the patients before treatment. As a result of their improvement, the patients were not only less confused, indifferent, and depressed, but showed better memory, greater motivation and initiative, and more sociable and cooperative behavior. In addition, the patients with such physical disturbances and dizziness, nocturnal cramps and paresthesias also exhibited significant improvement ($p < .05$).

The global change ratings indicated total clinical status was improved by the conclusion of the study in approximately one-half of the patients.

No significant changes in blood pressure occurred and no untoward effects were encountered for any

patient during the study. This is in agreement with the findings of other investigators (4-6), who reported no side effects.

Discussion

Study of the aging process and its attendant problems seems to be one of the more prominent areas of medical interest today. Until recently, "growing old" was generally considered as a persistent, degenerative "wearing out" of one's functional units — an inevitable occurrence. However, modern concepts of preventive medicine and more expectant attitudes towards rehabilitation are helping to change the focus of geriatric care.

The mere fact that aging constitutes a general catabolic process should not preclude the possibility that many of its overt manifestations could be allayed with proper medical attention. While much has been achieved through improved methods of comprehensive health care delivery, increasing the life span remains only a basic first step in caring for the aging patient.

With added years, geriatric patients experience physical, social and psychological problems which increasingly impair their ability to cope with the environment and to interact with people around them. Thus, health care for individuals over 65 (after the earning years) should be directed to preserving their capacities to function satisfactorily in activities of day-to-day life.

Our study with 29 geriatric patients has demonstrated that treatment with dihydrogenated alkaloids of ergot can help achieve this goal by relieving some of the disconcerting and sometimes incapacitating symptoms of cerebrovascular insufficiency. Our patients experienced both clinically and statistically significant improvements in a number of the items rated. This usually meant less frequent or severe dizziness and cramps, less confusion and depression, greater mental alertness, and more sociability and cooperativeness.

When one considers the limited functioning inherent in a population as old as those included in this study, the improvements obtained with this medication become even more impressive. It might also be worthwhile to

observe the effects of the drug in patients just beginning to show the symptoms of CVI. Perhaps, as in the treatment of other conditions, rapid therapeutic intervention at the onset would have the greatest salutary effect.

Summary

Twenty-nine geriatric patients with symptoms of cerebrovascular insufficiency (CVI) completed 12 weeks of treatment with dihydrogenated alkaloids of ergot. Patients received 2 tablets (0.5-mg) sublingually three times a day, before or after meals. The criteria of drug effect were changes observed in commonly occurring manifestations of CVI, an overall impression of therapeutic effect, and an evaluation of the patients' global change. Analysis of the data revealed, in general, beneficial effects in the patients' psychological, social and physical manifestations. No untoward effects were observed.

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ANALISIS DEL LIBRO: "GUÍA TERAPEUTICA DE URGENCIA,
VOLUMEN II. EDITORIAL CIENTIFICO MEDICA
POR EL PROFESOR B. LORENZO VELAZQUEZ

El Profesor Lorenzo Velázquez es muy conocido de la profesión médica de Puerto Rico porque tiene aquí cientos de discípulos. Los otros compañeros que no fueron sus discípulos pudieron conocerle cuando vino invitado a Puerto Rico. Fue uno de los profesores cuyas conferencias en la Universidad y la Asociación Médica cargadas de novedad y de docencia dejaron un recuerdo imborrable en cuantos las escuchamos.

Su última edición (1970) de su *Terapéutica y Farmacología Experimental* en 2 tomos es sin duda alguna la mejor obra de su clase publicada en castellano y una de las mejores de entre todos los idiomas.

Acaba de publicar la 14 edición de su "Guía Terapéutica de Urgencia" revisando las anteriores ediciones y actualizándola. Lo ha impreso en papel biblia, y en formato de bolsillo de tal manera, que sea fácil llevarlo consigo el médico y especialmente el G. P. llamado para un caso de emergencia.

Las normas generales que el Profesor Velázquez recomienda seguir son: Diagnóstico cierto, y después "dar bien, dar rápido y dar fuerte".

En la urgencia cada minuto cuenta, por eso hay que

llegar con las armas terapéuticas indicadas antes de que el paciente se haga irrecuperable.

A la cabeza de cada tópico constan unas orientaciones clínicas que pueden ser decisivo recordatorio para hacer el diagnóstico cierto, seguidas de las orientaciones terapéuticas así como las contraindicaciones. Se ha incluido en esta parte todo aquello que de actualidad ha surgido y ha sido comprobado con visus de marcada utilidad y provecho hasta junio de 1971.

Ejemplos del índice alfabético de materias: A, abejas (picaduras), termina Aspirina (intoxicación), C, Cerebro (embolia) termina Culebras (picaduras), E, Eclampsia infantil, termina Estreptomicina (Alergia a la), H, Hematemesis, termina: Hipertensión arterial parosistita, P, Pancreatitis aguda, termina, Pulmón (hemorragias), T, Taquicardia paroxística, termina, Trombosis vasculares...

Yo dejo en la Biblioteca de nuestra Asociación Médica un ejemplar de esta Guía Terapéutica de Urgencia para que pueda ser examinado por los compañeros que tengan interés en ella.

A. Rodríguez Olleros, MD

NOTICIAS

We reproduce below letter received from the Hospital Director of the Emily P. Bissell Hospital, at 3000 Newport Cap Pike, Wilmington, Delaware 19808, for the benefit of those interested:

"We, in Delaware with the Division of Public Health, Department of Health & Social Services, have interesting and challenging opportunities for a Medical Director and several staff physicians at Emily P. Bissell Hospital. This hospital, which is pleasantly located in the suburban Wilmington area, provides for the treatment and rehabilitation of tuberculosis and chronically ill patients. A new program, the comprehensive rehabilitation of the physically disabled adult, is being developed."

These positions are covered under the Satte Merit System with salaries ranging up to \$28,000 (plus housing with all utilities), depending on training and experience. The State has a very liberal vacation, sick leave and retirement plan, plus many other fringe benefits."

"Delaware, by virtue of its four seasons and its ideal location on the mid-Atlantic coast, offers many cultural and recreational attractions. Many metropolitan cities can be reached within two (2) hours' driving time. Low taxes and a strong economy are other attributes of the State. There is no general sales tax!" "Delaware enjoys one of the finest public educational systems in the nation".

"If you know any physicians who might be interested in these positions, please call me collect on 302-908-2223, extension 202, or write to me at the above address, and we will arrange an interview at a mutually agreeable time".

From the HEW News:

Under a ruling from the Price Commission, a required increase in the Medicare hospital deductible was cut in half from \$8 to \$4, Secretary of Health, Education, and Welfare Richardson announced today.

Beginning January 1, 1973, a Medicare beneficiary will be responsible for the first \$72 of his hospital bill, a reduction of 5 1/4 percent from the rate which otherwise would have applied. The present rate is \$68.

In absence of action by the Price Commission, Secretary Richardson said that the portion of the hospital bill for which a Medicare beneficiary is responsible would have gone from \$68 to \$76, based on a mathematical formula in the Medicare law which does not leave him any administrative discretion. The law requires the Secretary of Health, Education, and Welfare to announce an increase in the deductible amount for each calendar year based on the most recent level of Medicare hospital costs for which annual data is available, in this case, 1971.

Prior to formal announcement of the 1973 rate, Secretary

Richardson said he asked the Cost of Living Council to determine if the hospital deductible was subject to the provisions of the Economic Stabilization Program. The Council ruled that the deductible represents a price paid by Medicare recipients for hospital services and that it is, therefore, governed by Price Commission regulations limiting the increase in prices which can be charged by institutional provider of health services. The Price Commission, therefore, held the increase to 6 percent, based on Section 6 C.F.R. 300.18 of its regulations.

Medicare's hospital deductible is subject to periodic adjustment to reflect changes in average daily costs of hospital care under the program. The current increase, based on 1971 data, reflects in part costs incurred prior to the Economic Stabilization program and, as well, includes cost increases resulting from more advanced and expensive technology in hospitals as well as general increases in costs of goods and services.

Secretary Richardson said that when the hospital deductible amount changes on January 1 of each year, the law requires that comparable changes be made in the dollar amounts a Medicare beneficiary pays toward a hospital stay of more than 60 days, or a posthospital extended care stay of more than 20 days.

When a Medicare beneficiary has a hospital stay of more than 60 days, he will pay \$18 a day for the 61st through the 90th day, up from the present \$17 per day. If he has a posthospital stay of over 20 days in an extended care facility, he will pay \$9 per day toward the cost of the 21st day through the 100th day, up from the present \$8.50 per day.

If he needs to draw on his "lifetime reserve" the reserve of hospital days a beneficiary can draw upon if he ever needs more than 90 days of hospital care in the same benefit period, he will pay \$36 for each day used, instead of the present \$34 per day.

Secretary Richardson noted that the Cost of Living Council, in conjunction with the Health Services Industry Committee, the Price Commission, and other appropriate agencies, is proceeding with a staff study on health care costs with particular emphasis on hospitals and health insurance. The objective of the study is to come up with improved ways of controlling the cost of health care while still maintaining the quality of care.

THE AMERICAN BOARD OF FAMILY PHYSICIANS announces that it will give its next two-day written certification examination on October 20-21, 1973. It will be held in various centers geographically distributed throughout the United States. Information regarding the examination can be obtained by writing:

Nicholas J. Pisacano, MD, Secretary
American Board of Family Practice, Inc.
University of Kentucky Medical Center
Annex No. 2, Room 229
Lexington, Kentucky 40506

PLEASE NOTE: It is necessary for each physician desiring to take this examination to file a completed application with the Board office. Deadline for receipt of applications in this office is August 1, 1973.

From the American Academy of Family Physicians News:

MORE THAN 1,000 TRAINING IN FAMILY PRACTICE RESIDENCIES — Kansas City, MO. - The American Academy of Family Physicians' recent annual survey of family practice residency programs shows that 1,015 young graduates are training to be family physicians.

This figure almost doubles the number enrolled in family practice residency programs a year ago. It is three times more than were in training in 1970.

The survey also indicates that 81 percent of the available first-year family practice residency slots are filled, bettering by 10 percent the figure in 1971. This percentage of filled first-year slots is higher than that for most other medical specialties.

Three years ago, there were 20 approved programs. There now are 107. Currently there are 34 departments and 31 divisions of family practice in the nation's 105 medical schools.

Title of Program: "Controversial Issues in Pediatric Cardiology, 1973"

Sponsor: University of Miami School of Medicine, Division of Pediatric Cardiology

Program Director: Sidney Blumenthal, MD, Professor of Pediatric Cardiology, Associate Dean for Continuing Education

Dates: March 19-22, 1973.

Place: Sonesta Beach Hotel, Key Biscayne, Florida

Fee: \$125.00

\$ 50.00 Fellows (with certification of Chief of Service)

Inquiries: Division of Continuing Education, University of Miami School of Medicine, P. O. Box 875, Biscayne Annex, Miami, Florida 33152.

News Release from the Industrial Medical Association and the American Association of Industrial Nurses:

The 1973 American Industrial Health Conference will be held April 16 - 19 at Currihan Hall in Denver, Colo., with headquarters at the Denver-Hilton Hotel, it has been announced by the INDUSTRIAL MEDICAL ASSOCIATION and the AMERICAN ASSOCIATION OF INDUSTRIAL NURSES. This

medical-nursing Conference which is comprised of the annual meetings of the two sponsoring organizations, will bring together approximately 2,500 persons including industrial physicians, industrial nurses, safety engineers, industrial hygienists, public health officials, academicians and management representatives.

The scientific program, in which many of the nation's experts in the field of occupational health will participate, will be augmented by both scientific and technical exhibits. Postgraduate seminars and workshops in selected areas of industrial medical practice also will be presented. Registration is open to anyone having an interest in the health of the working population. Registration fee is \$10.00. The advance program and registration forms, will be available in January from the American Industrial Health Conference, 150 North Wacker Drive, Chicago, Ill. 60606.

Through the courtesy of Peat, Marwick, Mitchell & Co., Certified Public Accountants, we quote below outstanding features of the tax legislation enacted in 1972 by the Puerto Rico Legislative Assembly:

INCOME TAXES:

Act No. 43 - Approved May 30, 1972

Under this Act real estate investment trusts are exempted from income taxes under certain conditions depending on the place of organization, as follows:

a) United States real estate investment trusts will be exempted provided they are treated as such real estate investment trusts under the United States Internal Revenue Code.

b) Real estate investment trusts organized in foreign countries will be exempted provided they are not required to pay in the foreign country any tax on their income from any source within Puerto Rico.

c) Real estate investment trusts organized in Puerto Rico. With respect to Puerto Rican investment trusts, the Secretary of the Treasury is empowered to issue rules and regulations governing (1) the formation, structure, activities and minimum number of shareholders of the trust; (2) the character and source of its income; (3) the composition, location and ownership of assets; (4) the tax treatment and nature of distributions to its shareholders and (5) the accounting records to be kept.

INDUSTRIAL INCENTIVE ACTS

Act. No. 9 - Approved June 8, 1972

This Act provides for a 50 percent tax exemption for guest houses or expansions thereof operated primarily in the interest of the tourist trade. Formerly, this 50 percent tax exemption was limited to commercial hotels.

The Act also introduces pertinent amendments to the Industrial Incentive Act of 1963 to include qualifying guest houses under the concept of "eligible business" and the income derived therefrom as "industrial development income." Guest houses qualifying for these purposes, however, are only those to which the Tourist Development Company has granted an appropriate certificate under Act. No. 10, approved June 18, 1970.

Act. No. 19 - Approved June 15, 1972

This Act clarifies the provisions of the Industrial Incentive Act of 1963 related to exemption for businesses located in the adjacent islands of Vieques and Culebra. The exemption period for such businesses remained in 25 years.

An amendment introduced by this Act allows the applicant for a tax exemption grant or to the exempted business itself up to the last day of the first year of exemption to make the election for the two-year deferral of the tax exemption period. Under prior law, the exempted business was required to make the election on or before the date fixed for the commencement of operations.

Other amendments introduced by Act. No. 19 added the following two new articles to the list of "designated articles" which may give rise to exempt manufacturing operations:

- 1) Every product which was manufactured in a commercial scale in Puerto Rico on or before January 2, 1947 for which production facilities existed in Puerto Rico on such date capable of producing it on a commercial scale, but which was not manufactured in Puerto Rico for the two calendar years immediately preceding the year 1972. An exemption for such a product can now be obtained provided the Governor of Puerto Rico determines that such exemption is necessary for the best interest of the Commonwealth of Puerto Rico.
- 2) Paperboard boxes and containers (except those made of corrugated paperboard).

This Act also expanded designated article No. 34 to include the publication of books, provided their printing is carried on in Puerto Rico. The rough printing and binding of any kind of book is also included. Prior provisions covered only the printing and binding of books on a commercial scale.

EXCISE TAX ACT

Act. No. 73 - Approved May 31, 1972

This Act exempts from excise taxes:

- a) Radio-telephone systems and their parts and accessories installed in taxicabs.
- b) New cars used as the working tool of the owner in the transportation of passengers for pay immediately after the acquisition.
- c) Any heavy motor vehicle registered for the first time in Puerto Rico by a person who, immediately after its acquisition, uses the vehicle for the transportation of loads for pay as his working tool.

PUERTO RICO EMPLOYMENT SECURITY ACT

Act. No. 16 - Approved June 15, 1972

This act introduced several amendments to the Puerto Rico Employment Security Act. The most significant of these amendments are summarized below:

- 1) Modifies the definition of employer by including any employment unit which during any day within the current or preceding calendar year has employed one or more individuals. The number of employees required to be considered an employer was not clearly stated before the amendment.

- 2) The Bureau of Employment Security is authorized to refer to a referee those decisions involving multiple claimants and presenting controversial issues of law and facts.
- 3) Provides that no bond deposit shall be necessary as a condition for initiating a judicial review procedure of a determination of rights to benefits or to file an appeal before the Supreme Court.

Postgraduate Course on "Neurophysiology and Treatment of Upper Motor Neuron Lesions" - March 19-23, 1973 at the Puerto Rico Medical Association Building in San Juan, Puerto Rico; co-sponsored by the American Academy of Physical Medicine and Rehabilitation:

March 19/73 - 8:00-10:00 pm - Sensori-Motor Organization of the Central Nervous System - This is a presentation of the hierarchic organization of the nervous system beginning with the rigid, stereotyped, spinal reflexes; the supraspinal reflexes and automatic facilitation of inhibition of the spinal reflexes; and finally the facile regulation of simple or complex function by the cerebrum.

March 20/73 - 8:00-10:00 pm - Spinal Reflexes - Here will be reviewed the spinal reflexes in an organized way pointing out the stimuli, pathways and responses and emphasizing how these appear in the human under normal and abnormal conditions.

March 21/73 - 8:00-10:00 pm - Supraspinal Reflexes - This will be a presentation of the supraspinal reflexes and their modification of spinal reflex function. The emphasis is primarily on the tonic neck and the labyrinthine reflexes. Movie records will be used to demonstrate these reflexes.

March 22/73 - 8:00-10:00 pm - Supraspinal Reflex Regulation and the Righting Reflexes - This lecture is concerned with facilitation and inhibition through the reticular formation, its influence in modifying spinal and supraspinal reflexes. The righting reflexes which are complex combinations of the body reflexes are presented in their functional manifestations and described in relation to use and training.

March 23/73 - 8:00-10:00 pm - Components of Treatment in Cerebral Palsy - This lecture puts together in an organized manner the components of therapy and management of the cerebral palsied patient: (1) prevention or correction of contractures; (2) establishment of normal tone; (3) establishment of psychomotor interaction with the environment; (4) establishment of normal postural control; (5) development of control in the prime movers of the extremities; (6) and training of coordination.

— A NUESTROS PATROCINADORES —

En este año a punto de terminar, la Junta Editora desea expresar su agradecimiento a nuestros patrocinadores del Boletín de la Asociación Médica de Puerto Rico, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos. Son éstos proveer un medio para la publicación de artículos científicos de nuestros médicos, informar a nuestros lectores de problemas médicos de importancia, proporcionar vías de comunicación para expresar puntos de vista; tanto oficiales como de índole personal, estimular liderato médico para la solución de nuestros problemas; en fin, lograr una revista de actualidad que refleje la calidad de la medicina Puertorriqueña.

Agradecemos la ayuda y apoyo de nuestros patrocinadores.

— TO OUR ADVERTISERS —

In this year about to end, the Editorial Board recognizes with gratitude the aid provided by those advertising in the Boletín de la Asociación Médica de Puerto Rico, whose support permits the fulfillment of our objectives. These are to provide the medium for publication of scientific articles by our physicians, to keep our readers informed of diverse medical problems of importance, to provide communication means for the expression of different points of view, to stimulate medical leadership for the solution of our problems, in short, to produce a journal which will reflect the quality of Puerto Rican medicine.

We sincerely thank our advertisers for their help and continued support.

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y no lo que deben...



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PR 5226.1 MAY, 1969

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Will his return to work mean the return of undue psychic tension?



When it's mandatory to keep the post-coronary patient calm, consider Valium (diazepam).

Although he's promised to take it easy back on the job, you know he's going back to the same stressful circumstances that may have contributed to his hospitalization. If he experiences excessive anxiety and tension because of overreaction to stress, your prescription for Valium can bring relief. During the period of readjustment Valium can quiet undue anxiety.

For moderate states of psychic tension, 5-mg or 2-mg Valium tablets *b.i.d.* to *q.i.d.* can usually provide reliable relief. For severe tension/anxiety

states, the 10-mg tablets often produce desired results.

The most commonly reported side effects are drowsiness, ataxia and fatigue. Until individual response is determined, caution patient against driving or operating dangerous machinery.

Valium® (diazepam)

For the tense cardiac patient who must be kept calm

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures.

Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision.

Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg *b.i.d.* to *q.i.d.*; alcoholism, 10 mg *t.i.d.* or *q.i.d.* in first 24 hours, then 5 mg *t.i.d.* or *q.i.d.* as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg *t.i.d.* or *q.i.d.*; adjunctively in convulsive disorders, 2 to 10 mg *b.i.d.* to *q.i.d.* **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg *t.i.d.* or *q.i.d.* initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

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ASOCIACION MEDICA DE PUERTO RICO

LONG TERM RESULTS OF INTERMITTENT STEROID TREATMENT IN THE ADULT NEPHROTIC SYNDROME 308

*José L. Cangiano, MD, Rafael Ramírez González, MD, Arturo Trevino, MS II, Rosa Lluberes, BS, MT, Jesús Vázquez, MD
Rodrigo Menéndez Corrada, MD and Osvaldo Ramírez Muxó, MD*

PATRON DE SELECTIVIDAD DE PROTEINAS EN ENFERMEDADES RENALES 314

*Rosa Lluberes, BS, Ph&MT, Arturo Trevino, MS, José L. Cangiano, MD, Osvaldo Ramírez Muxó, MD,
Rafael Ramírez González, MD y Rodrigo Menéndez Corrada, MD*

PRUEBA DE EXCRESION URINARIA DE XILOSA: UTILIDAD Y LIMITACIONES EN LA SEPARACION DE NIÑOS NORMALES DE PACIENTES CON ESPRU TROPICAL 319

Pedro J. Santiago Borrero, MD, Rafael Santini, Jr., PhD, Irma Ramírez, MD y Norman Maldonado, MD

LA PROFESION MEDICA ANTE LOS CAMBIOS QUE SE AVECINAN 323

Discurso

Félix S. Vilella Suau, MD

EDITORIAL 325

Acción y Reflexión

NOTA BIOGRAFICA DR. JOSE M. RIGAU MARQUES 328

CONTENIDO VOLUMEN 64 332

INDICE DE AUTORES 337

INDICE DE MATERIAS 340



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

Valium®
(diazepam)

To help you manage excessive psychic tension

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21 FEB 1973



the uncover girl...

Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for

Her contact dermatitis* cleared smoothly by **Vioform[®]-Hydrocortisone** (iodochlorhydroxyquin and hydrocortisone)

Nothing defeats today's abbreviated clothing styles like an exposed skin disorder. That's why physicians and patients have come to depend on the multiple benefits of Vioform-Hydrocortisone. Because it combines the antibacterial, antifungal actions of Vioform with the anti-inflammatory and antipruritic actions of hydrocortisone, Vioform-Hydrocortisone can prove effective in so many common skin disorders—where topical steroids alone can't cope with frequently coexisting bacterial or fungal infection.

antifungal • antibacterial • anti-inflammatory • antipruritic

*This drug has been evaluated as possibly effective for this indication. See brief prescribing information.



ns of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after continuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Adverse reports include: Hypersensitivity, local burning, irritation, pruritus. Continue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

USAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl

sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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C I B A

BOLETIN

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El Boletín se publica mensualmente. Todo material de anuncio está sujeto a aprobación por la Junta Editora.

Reimpresos:

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

Second Class postage paid at San Juan, Puerto Rico.

Should old depressives be forgot?

the geriatric depressive.

Unable to concentrate he tends to take little interest in the affairs around him. His reactions are slow and delayed. He speaks very little. When he does, it's mostly to complain of his insomnia, fatigue, or constipation.

One way of relieving depression in the geriatric patient is with Tofranil.

Please read the prescribing information for details of usage (lower dosages are recommended for elderly patients and adolescents), precautions, warnings, contraindications, adverse experiences, and dosage recommendations. It is summarized below.

Tofranil® Geigy imipramine hydrochloride USP



nil® imipramine hydrochloride USP

Contraindications: The concomitant use of this agent with monoamine oxidase inhibiting (M.A.O.I.) compounds is contraindicated. Hyperpyretic crises or convulsive seizures may occur. Potentiation of these effects can be serious or even fatal. An interval of at least 14 days after M.A.O.I. therapy has been discontinued should be allowed before this drug may be substituted. Initial dosage should be low, increases should be gradual, and the patient's progress should be carefully observed. The drug is also contraindicated during the acute recovery period after myocardial infarction. (b) in patients with known hypersensitivity to the drug. Cross-sensitivity to other dibenzamine compounds should be kept in mind.

Warnings: *Usage in Pregnancy:* Safe use of imipramine during pregnancy and lactation has not been established; therefore, in administering the drug to pregnant patients, nursing mothers, or women of bearing potential, the potential benefits must be weighed against the possible hazards. Animal reproduction studies have yielded inconclusive results. There have been clinical reports of congenital malformation associated with the use of this drug, but a causal relationship has not been confirmed. Extreme caution should be used when this drug is given to:

patients with cardiovascular disease because of the possibility of conduction defects, arrhythmias, myocardial infarction, strokes and tachycardia; patients with increased intraocular pressure, history of urinary retention, or history of narrow-angle glaucoma because of the drug's anticholinergic properties; elderly thyroid patients or those on thyroid medication because of the possibility of cardiovascular toxicity; patients with a history of seizure disorder because the drug has been shown to lower the seizure threshold;

patients receiving guanethidine or similar agents as imipramine may block the pharmacologic effects of these drugs. Pending evaluation of results from clinical trials in children, the drug is not recommended for use in patients under twelve years of age. The drug may impair the mental and/or

physical abilities required for the performance of potentially hazardous tasks, such as operating an automobile or machinery, the patient should be cautioned accordingly.

Precautions: Because of the possibility of suicide in seriously depressed patients, careful supervision during the early phase of treatment is necessary and hospitalization may be required. Prescriptions should be written for the smallest amount feasible.

Hypomanic or manic episodes may occur, particularly in patients with cyclic disorders. Such reactions may necessitate discontinuation of the drug. If needed, imipramine may be resumed in lower dosage when these episodes are relieved. Administration of a tranquilizer may be useful in controlling such episodes.

Prior to elective surgery, imipramine should be discontinued for as long as the clinical situation will allow.

An activation of the psychosis may occasionally be observed in schizophrenic patients and may require reduction of dosage and the addition of a phenothiazine.

In occasional susceptible patients or in those receiving anticholinergic drugs (including antiparkinsonism agents) in addition, the atropine-like effects may become more pronounced (e.g. paralytic ileus). Close supervision and careful adjustment of dosage is required when this drug is administered concomitantly with anticholinergic or sympathomimetic drugs.

Patients should be warned that the concomitant use of alcoholic beverages may be associated with exaggerated effects.

Both elevation and lowering of blood sugar levels have been reported.

Concurrent administration of imipramine with electroshock therapy may increase the hazards; such treatment should be limited to those patients for whom it is essential.

Adverse Reactions: *Cardiovascular:* Hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, stroke, falls.

Psychiatric: Confusional states (especially in the elderly) with hallucinations, disorientation, delusions; anxiety, restlessness, agitation; insomnia and nightmares; hypomania; exacerbation of psychosis.

Neurological: Numbness, tingling, paresthesias

of extremities; incoordination, ataxia, tremors; peripheral neuropathy; extrapyramidal symptoms; seizures, alterations in EEG patterns; tinnitus.

Anticholinergic: Dry mouth, and, rarely, associated sublingual adenitis; blurred vision, disturbances of accommodation, mydriasis; constipation, paralytic ileus; urinary retention, delayed micturition, dilation of the urinary tract.

Allergic: Skin rash, petechiae, urticaria, itching, photosensitization (avoid excessive exposure to sunlight); edema (general or of face and tongue), drug fever, cross-sensitivity with desipramine.

Hematologic: Bone marrow depression including agranulocytosis; eosinophilia; purpura; thrombocytopenia. Leukocyte and differential counts should be performed in any patient who develops fever and sore throat during therapy; the drug should be discontinued if there is evidence of pathological neutrophil depression.

Gastrointestinal: Nausea and vomiting, anorexia, epigastric distress, diarrhea; peculiar taste, stomatitis, abdominal cramps, black tongue.

Endocrine: Gynecomastia in the male; breast enlargement and galactorrhea in the female; increased or decreased libido, impotence; testicular swelling; elevation or depression of blood sugar levels.

Other: Jaundice (simulating obstructive); altered liver function; weight gain or loss; perspiration; flushing; urinary frequency; drowsiness, dizziness, weakness and fatigue; headache; parotid swelling; alopecia.


Withdrawal Symptoms: Though not indicative of addiction, abrupt cessation of treatment after prolonged therapy may produce nausea, headache and malaise.

How Supplied: Round tablets of 25 and 50 mg.; triangular tablets of 10 mg. for geriatric and adolescent use; and ampuls, each containing 25 mg. in 2 cc. for I.M. administration. (B)98-146-850-H (7/71)

For complete details, including dosage, please refer to the full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

TO 8575



**if skin is infected,
or open to infection...
choose the topical
that gives your patient—**

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin[®] Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
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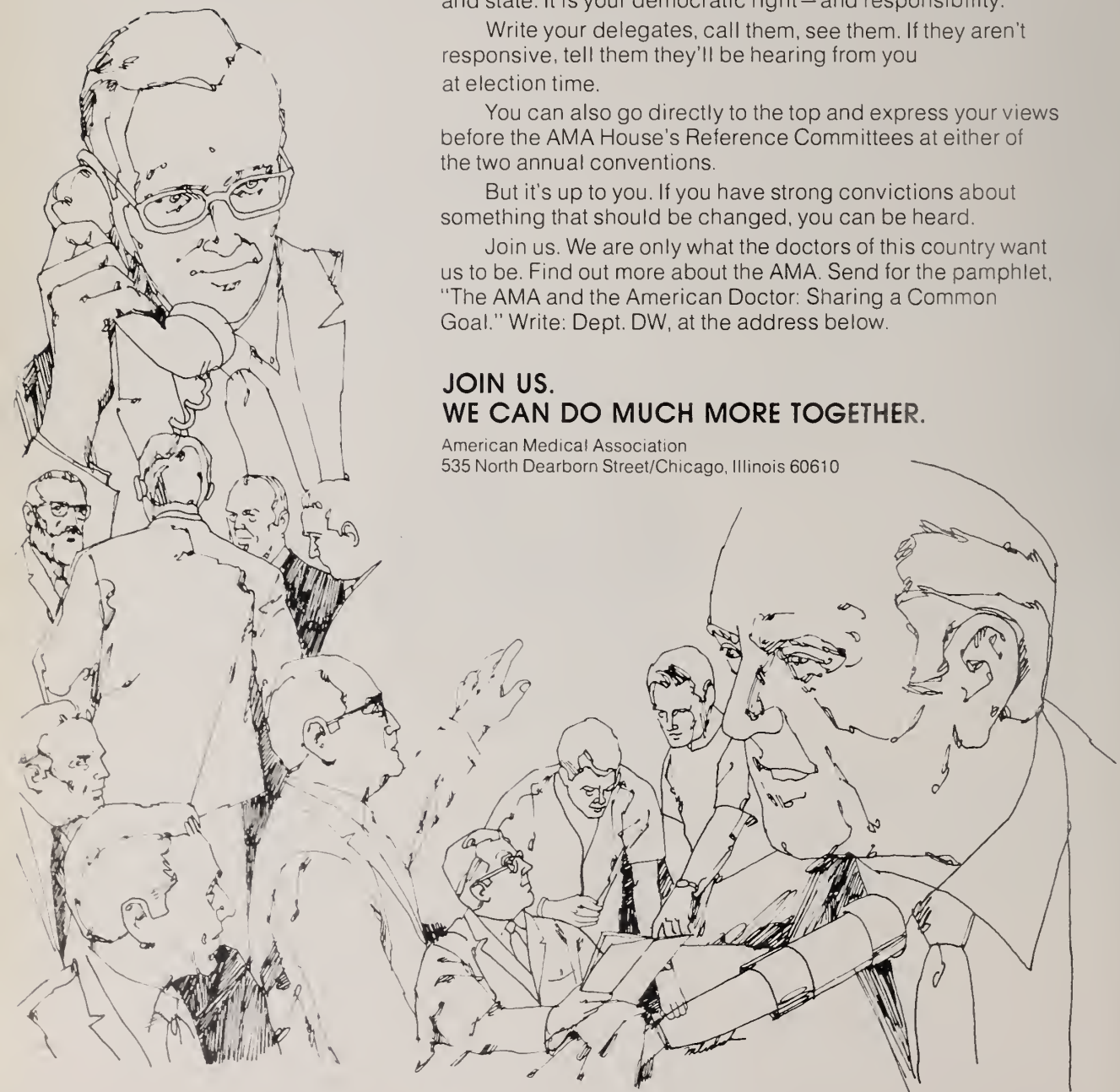
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LONG TERM RESULTS OF INTERMITTENT STEROID TREATMENT IN THE ADULT NEPHROTIC SYNDROME

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It is of grave concern that a large number of adult nephrotic patients, unlike most childhood nephrotics, develop gradual deterioration of renal function ultimately leading to disability and death. The cost of dialytic techniques to maintain patients with chronic renal failure is enormous and in many instances prohibitive. Therefore, it is of utmost importance for the clinician to prevent or significantly delay the development of renal functional impairment. Nephrotic patients with normal or minimal changes in biopsy specimens will benefit from steroid therapy. Similarly, patients with highly selective proteinuria consisting mainly of albumin are more likely to benefit from corticosteroids. However, in a large number of patients the nephrotic syndrome is associated with proliferative, purely membranous or membranoproliferative glomerulonephritis. The results of steroid therapy have been equivocal. Accordingly, this study attempted to define the response to long term intermittent steroid therapy in patients with purely membranous, proliferative or membranoproliferative glomerulonephritis. In addition we tried to establish a correlation between selectivity of protein clearance and the response to therapy.

Methods

Thirteen adult patients with idiopathic nephrotic syndrome were studied, excluding lupus erythematosus, diabetes mellitus, amyloidosis, renal vein thrombosis, drug reaction or acute glomerulonephritis. Schreiner's criteria (1) for nephrotic syndrome were used, namely, urinary protein excretion of 3 grams per 24 hours or more, hypoalbuminemia and variable degrees of edema. All patients had a creatinine clearance of 44 ml per minute per 1.73 m² of surface area or more. Of the 13 patients, 11 were males and 2 females; 11 were white and 2 negro. Their

age ranged from 26 to 62 years (mean 38). Prior to treatment histological diagnosis was made from tissue obtained by percutaneous needle biopsy using an image amplifier. The renal tissue was processed with buffered formalin and stained with hematoxylineosin; Masson trichrome, periodic acid Schiff (PAS) and PAS methenamine silver stains. Eight patients showed membranoproliferative glomerulonephritis and 5 showed a purely membranous glomerulonephritis. Prednisone, 40 to 80 mg every other day was given to all patients for periods of 12 to 26 months. A repeat percutaneous biopsy was performed at the end of the treatment period. The following studies performed before treatment, at bimonthly intervals and at the end of the treatment period: 24 hour creatinine clearance, total proteins, serum albumin and globulin and 24 hour urinary proteins. In addition filter paper electrophoresis (Beckman) and double immunodiffusion for screening of proteins in the urine were performed. Immunoglobulins were determined by the simple radial diffusion immunoplate method (Hyland Laboratories, Los Angeles, California). Protein clearances were calculated according to the general formula $\frac{UV}{P}$. Absolute clearances were expressed as microliters per minute $\times 10^3$ for ease of representation on double logarithmic paper. Clearances were also calculated as percentage of the individual clearances of transferrin in an attempt to standardize the values obtained. The percentage values are plotted against respective molecular weights on a log graph. A straight line was estimated by the method of least squares, and a slope determined. The angle (θ) is derived from the slope, the tangent of (θ), and expressed as degree of selectivity. When small amounts of high molecular weight protein are excreted the slope is flatter and the

TABLE 1: CLINICAL CRITERIA OF RESPONSE

1. Excellent	- complete clinical remission with proteinuria less than 300 mg per 24 hour and normal creatinine clearance (>100 cc/min/1.73 m ²)
2. Good	- a) Proteinuria less than 1.25 gm per day b) a 50 percent or more drop in proteinuria c) a less than 15 percent reduction in creatinine clearance
3. Poor	- No significant improvement in proteinuria or creatinine clearance by the above criteria.

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Presented at the 69th Annual Meeting of the Puerto Rico Medical Association in San Juan, P. R., Nov. 1971.

TABLE II

Patient	Kidney Pathology	BEFORE TREATMENT		Prednisone dose mg q.o.d.	AFTER TREATMENT	
		Urine Protein grams/day	Creat. Clearance ₂ cc/min/1.73 m ²		Protein grams/day	Creat. Clear. ₂ cc/min/1.73 m ²
1	MP	12.8	58	80	8.7	99
2	MP	8.3	139	80	4.13	134
3	MP	9.6	115	80	6.3	123
4	M	7.7	63	60	7.7	61
5	MP	10.6	47	60	3.7	49
6	MP	3.0	110	80	2.2	131
7	M	20.0	50	80	25.0	41
8	M	8.4	120	80	6.5	110
9	M	12.0	150	80	17.0	120
10	MP	3.7	85	60	2.6	97

MP - membranoproliferative

M - membranous

TABLE III

Patient	Kidney Pathology	BEFORE TREATMENT		Prednisone dose mg q.o.d.	AFTER TREATMENT	
		Urine Protein grams/day	Creat. Clearance ₂ cc/min/1.73 m ²		Protein grams/day	Creat. Clear. ₂ cc/min/1.73 m ²
11	MP	3.6	98	80	1.16	117
12	MP	8.4	130	40	0.5	132
13	M	8.0	44.1	40	0.8	75

MP - membranoproliferative

M - membranous

proteinuria is unselective. Poor selectivity is defined as an angle of less than 60 degrees (2).

The clinical criteria of response was divided into excellent, good or poor based on proteinuria and glomerular filtration rate (Table 1).

Results

Clinical Response to Steroid Therapy

None of the 13 patients studied had an excellent response, 3 had a good response and 10 had a poor response (Tables II and III). The 3 patients with a good clinical response also demonstrated improvement in histological findings. Patients with poor response did not show any histological improvement at the end of the treatment period. Of the 3 patients with good response, 2 had membranoproliferative glomerulonephritis. One had purely membranous glomerulonephritis

and was also receiving warfarin (coumadin) because of recurrent pulmonary emboli. No evidence of renal vein thrombosis or a hypercoagulability state was present in this patient. An illustrative example of the clinical course and histological findings in a patient with a good response is depicted in figures 1, 2 and 3. No deleterious side effects of prednisone were observed during the treatment period.

Selectivity of Protein Clearance and Response to Therapy

All patients demonstrated a low degree of selectivity of protein clearances, predominantly excreting large amounts of albumin, IgG and IgA. Figure 4 shows the serum, urine and clearance patterns of IgG, IgA and IgM in a patient with a good response to prednisone therapy. IgG and IgA consistently appeared in the urine without correlation between response to therapy

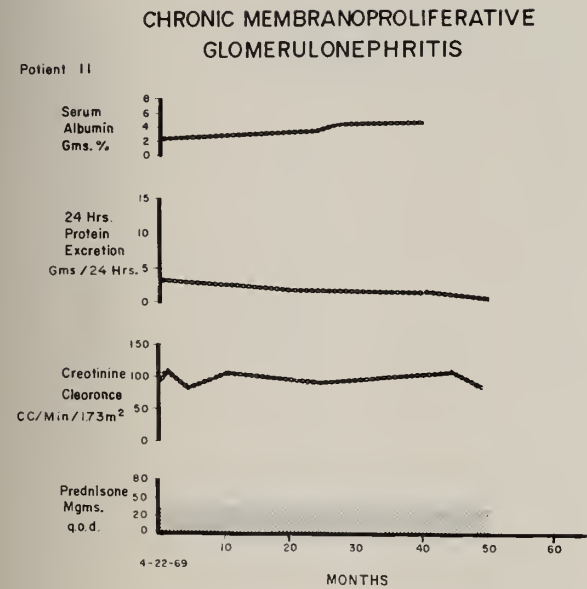


Fig. 1: Clinical course of a patient with good response (patient 11).

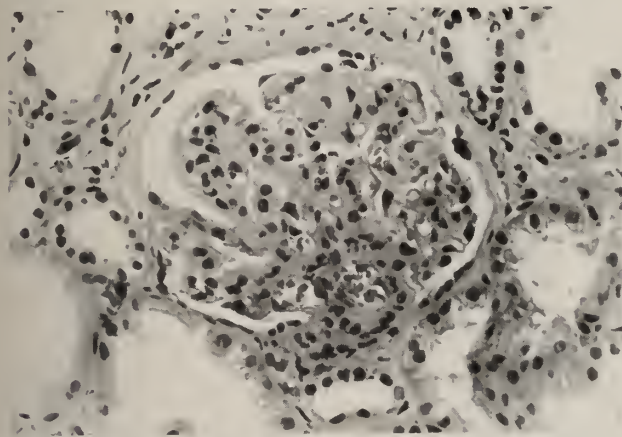


Fig. 2: Membranoproliferative changes before prednisone therapy (patient 11).

and protein clearance. Figure 5 shows the serum and urine levels and clearance of immunoglobulins in a patient who responded poorly to treatment. Initially the clearances are very high but later as the treatment progresses, the urine immunoglobulins have a tendency to decrease while the serum immunoglobulins are maintained at low levels. This pattern suggests but does not prove deposition of immunoglobulins in the basement membrane of the glomerulus. In Table IV the selectivity slope of all patients is analyzed before

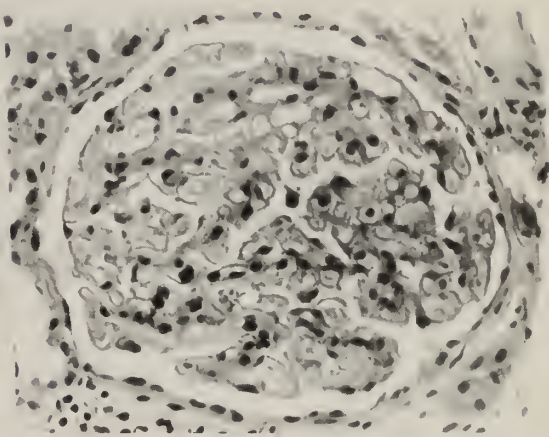


Fig. 3: Moderate improvement in glomerular changes after prednisone therapy (patient 11).

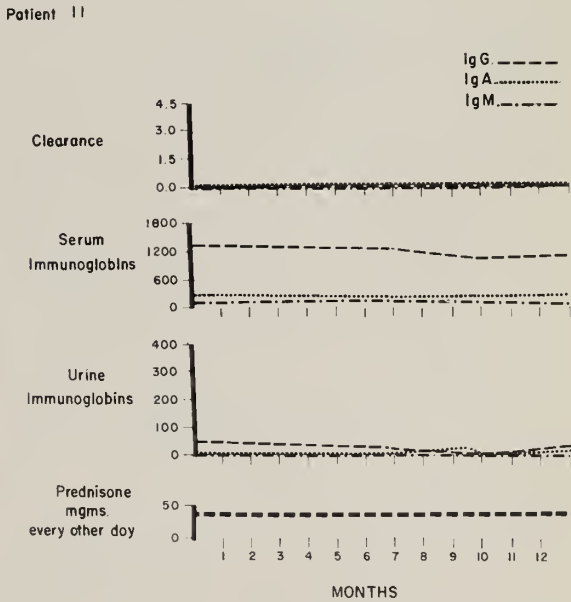


Fig. 4: Serum urine and clearance patterns of immunoglobulin in a good responder to prednisone (patient 11).

and after treatment with prednisone. Except for two patients (patients 12 and 13) in whom no transferrin was detected in the urine and the slope was not determined, there was a definite direct correlation between a poor selectivity slope and no response to therapy. The slope was reproducible in all patients and steroid therapy did not alter the slope in most patients. Interestingly, patient 11 demonstrated no change in the selectivity despite decrease in proteinuria. Figures 6 and 7 show the selectivity slope in a poor

TABLE IV: SELECTIVITY SLOPE IN THE NEPHROTIC SYNDROME

Patient	Before Treatment	After Treatment	Response	Pathology
1	50°	51°	P	MP
2	55°	54°	P	MP
3	56°	50°	P	MP
4	52°	51°	P	M
5	53°	49°	P	MP
6	56°	52°	P	MP
7	46°	42°	P	M
8	28°	41°	P	M
9	48°	48°	P	M
10	51°	58°	P	MP
11	50°	50°	G	MP
12	46°	*	G	MP
13	50°	*	G	M

P - poor
G - good
MP - membranoproliferative
M - membranous
* - no transferrin detected

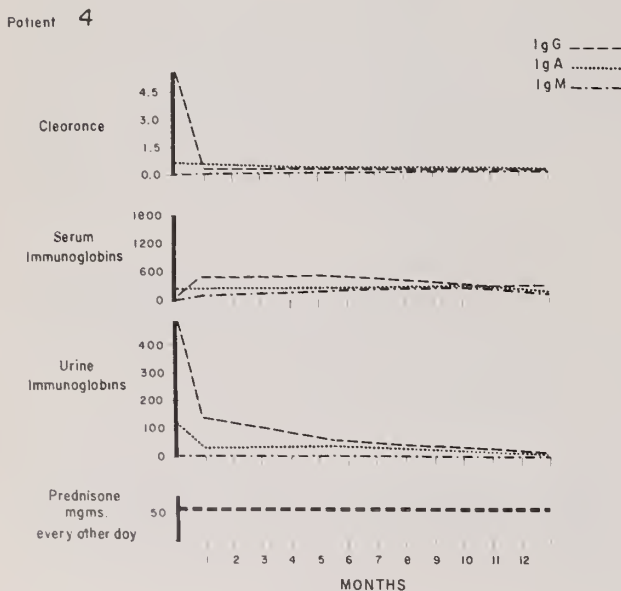


Fig. 5: Serum, urine and clearance patterns of immunoglobulin in a poor responder (patient 4).

responder before and after prednisone.

Discussion

Our results with long term intermittent prednisone therapy in 13 patients with adult idiopathic nephrotic

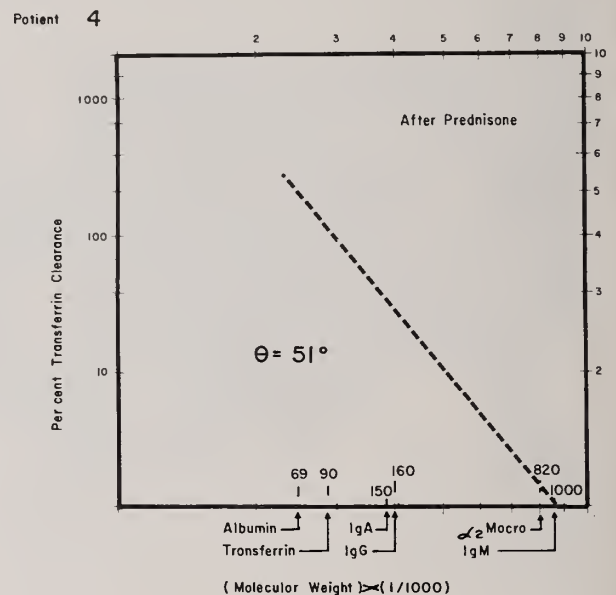


Fig. 6: Selectivity slope before prednisone therapy (patient 4).

syndrome demonstrated a poor result in 10 and a good response in 3 patients. No excellent response according to our clinical criteria for improvement was observed. The histological findings of these patients were those of membranous and membranoproliferative glomerulonephritis. A similar experience has been reported by other investigators (3, 4) treating membranous or

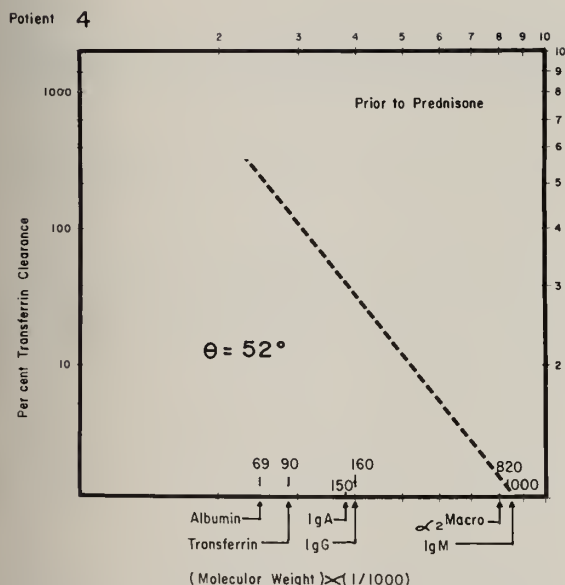


Fig. 7: Selectivity slope after prednisone therapy (patient 4).

proliferative glomerulonephritis with steroid therapy alone. In addition Black, Rose and Brewer (5) recently reported in 125 nephrotic patients the failure of response to steroid treatment in the membranous and proliferative lesions. The consensus is that steroids produce a uniformly, excellent response in the "minimal change" lesion, which rarely occur in adults. In our group of patients we have not observed cases of "minimal change" glomerulonephritis or adult lipid nephrosis.

The predisposition of one of our patients to suffer recurrent episodes of pulmonary embolism is not altogether unusual. Kendall *et al* (6) reported three nephrotic patients with pulmonary embolism secondary to lower limb or caval thrombosis. Their findings suggested a hypercoagulable state in 35 non-azotemic nephrotic patients with elevated levels of plasma fibrinogen, factor V, combined VII and X and VIII, mild thrombocytosis and accelerated thromboplastin generation. Anticoagulant therapy was given to two of them with a reversal of coagulation profile to normal and a clinical remission of their nephrotic syndrome. No laboratory evidence of a hypercoagulable state has been found in our patients. After partial remission, steroid therapy was discontinued and warfarin alone has been given for the past one year which has maintained a good clinical response. Our most recent data show proteinuria of less than 1 gm per 24 hours and increase of creatinine clearance from pre treat-

ment levels. These observations suggest that carefully controlled trials should be initiated to determine the therapeutic value of anticoagulant therapy in adult nephrotic syndrome.

The selectivity of proteinuria has been used to assess "pore size" or glomerular permeability and predict response to therapy. Blainey, *et al* (7) reported that patients with minimal change lesions had the highest selectivity and the membranous lesion was the least selective. Joachim *et al* (8) showed a direct relationship between clinical response to steroid therapy and selectivity of proteinuria. Our findings of unselective proteinuria in all patients correlated with biopsy findings of membranous and membrano proliferative lesion. No characteristic selectivity pattern was found for a given pathologic lesion although there was a tendency of the idiopathic purely membranous glomerulonephritis to be the least selective. In addition a correlation between selectivity of proteinuria and no response to therapy was seen. The observation of unchanged selectivity despite decrease in proteinuria after prednisone in one of our patients may indicate that the "defect" may persist and implies that steroids may reduce proteinuria by a mechanism other than changing pore size.

In conclusion, long term steroid therapy for 12 to 26 months is not completely effective in reversing the abnormalities associated with the membranous and membrano proliferative glomerulonephritis. At present we feel other forms of therapy, namely, immunosuppressive treatment with azathioprine or cyclophosphamide should be investigated. However, we need more controlled studies before we would recommend these for the treatment of nephrotic syndrome associated with membranous or membrano proliferative glomerulonephritis.

Summary

Thirteen adult patients with membranous and membrano proliferative glomerular lesions associated with a nephrotic syndrome were treated with intermittent steroid therapy for periods of 12 to 26 months. None of the 13 patients had an excellent response; 3 had a good response and 10 had a poor response following our clinical criteria. Histological findings correlated with the clinical response. All patients showed a poor selectivity of proteinuria. A correlation between poor selectivity of proteinuria and no response to steroid therapy was found. Based on these studies we conclude that long term steroid therapy is not altogether effective

in reversing the abnormalities associated with membranous and membrano-proliferative glomerulonephritis in the adult nephrotic syndrome.

Resumen

Trece pacientes adultos con lesiones glomerulares de tipo membrano-proliferativo asociado a un síndrome nefrótico fueron tratados intermitentemente con prednisona. Ninguno de los 13 pacientes obtuvo una respuesta clínica excelente. De acuerdo a nuestro criterio clínico 3 pacientes obtuvieron una buena respuesta y 10 pacientes no respondieron. Todos los pacientes demostraron una pobre selectividad en la excreción de proteínas. Se demostró una correlación entre la selectividad pobre de excreción de proteína y la respuesta a prednisona. Basándonos en estos estudios concluimos que la terapia prolongada con prednisona no es completamente efectiva en revertir las anomalías clínicas asociadas con lesiones glomerulares membranosas y membrano-proliferativa en el síndrome nefrótico del adulto.

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PATRON DE SELECTIVIDAD DE PROTEINAS EN ENFERMEDADES RENALES

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Aunque generalmente se acepta que proteinuria es el resultado de un aumento en la permeabilidad de la membrana glomerular, no se conoce el mecanismo responsable por su excreción. La permeabilidad de la membrana glomerular en la proteinuria moderada o severa se ha interpretado como función de la distribución del tamaño de los poros de esta membrana (1, 2). Este concepto sugiere la presencia de alteraciones en el tamaño de los poros de la membrana glomerular que permite el paso de las proteínas al filtrado glomerular (3).

Pappenheimer (4) y Brewer (5) infundieron dextran de varios pesos moleculares encontrando que la distribución del tamaño de los poros en el glomérulo normal correspondía a dextran de peso molecular de 5,000 a 85,000. Estos hallazgos sugieren fuertemente una estrecha relación entre la depuración de proteínas y su peso molecular (6). A pesar de esta relación con glomerulos normales, no se ha encontrado un patrón característico de selectividad en enfermedades renales, ya que los pacientes con cambios glomerulares histológicos avanzados parecen tener una menor selectividad en excreción de proteínas (3). Las lesiones glomerulares así como las tubulares, pueden presentar una magnitud de proteinuria tal que impida diferenciar si esta proteinuria la origina una lesión tubular, una lesión membranosa o una lesión membrano-proliferativa. El propósito de nuestro trabajo ha sido corroborar estos hallazgos o ver si en realidad existe una relación entre el patrón de selectividad excretoria de proteínas según su identificación inmunológica y ciertas enfermedades renales.

Las proteínas del suero sanguíneo han sido identificadas y clasificadas mediante métodos químicos y electroforéticos convencionales. Las fracciones identificables por estos métodos se les ha llamado albúmina, globulina

alfa-1, globulina alfa-2, beta globulina y gama globulina. Hay ciertas fracciones de las proteínas presentes en el suero que no pueden ser diferenciadas por estos métodos convencionales ya que poseen movilidad electroforética similar. Métodos sensitivos y reproducibles como el de inmunodifusión radial (7) han sido desarrollados para identificar y cuantitizar estas fracciones de las proteínas y mediante los cuales se han podido identificar las inmunoglobulinas (Igs). Estas inmunoglobulinas son un conjunto de proteínas séricas con propiedades de anticuerpo (independiente de su especificidad, afinidad o tipo). Este método ha proporcionado a los investigadores los medios adecuados para estudiar la depuración de inmunoproteínas por el riñón, permitiendo desarrollar la base del concepto de la selectividad excretoria.

Material y Métodos

La depuración de seis proteínas fueron estudiadas en 26 pacientes renales, 16 de los cuales padecían de un síndrome nefrótico documentado por biopsia percutánea, mientras que 10 pacientes presentaron lesiones de tipo preponderantemente tubular (pielonefritis crónica y riñón poliquístico).

Los pacientes con lesiones primordialmente glomerulares fueron subdivididos de acuerdo a las características de la histopatología en un grupo con lesiones membranosas y otros con lesiones membrano-proliferativas.

La concentración en el suero y orina de IgG, IgA, y IgM, transferrina, albumina y macroglobulina alfa-2 se determinó por inmunodifusión radial simple utilizando placas de agar-anticuerpo comerciales (Immunoplates, Hyland Lab., Los Angeles, California).

Cada serie de determinaciones se comparó contra curvas de referencia producidas de 3 o 4 standard diferentes conocidos, la gráfica es la expresión de la relación que existe entre el diámetro del anillo de precipitación de inmunoglobulina y su concentración. Una familia de curvas se determinó para cada fracción de proteínas a investigar. El diámetro del anillo fue medido con un visor de pequeño aumento (Viewer). Bajo estas mismas condiciones, los valores normales y el coeficiente de variación para concentraciones de inmunoglobulinas fue de $1,510 \pm 204.3$ mg/100 ml para IgG, 325 ± 77 mg/100 ml para IgA, 103 ± 33.5 mg/100 ml para IgM (8). Los valores obtenidos son el promedio de 69 determinaciones realizadas en suero de personas libres de enfermedades renales encontrándose que son similares a las comunicadas por otros auto-

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res. La depuración de proteínas fue calculada por la fórmula clásica $C = UV$.

Resultados

Al comparar los niveles de las inmunoglobulinas séricas G, A, y M de normales con los de los pacientes con lesiones glomerulares podemos notar que en aquellos con lesión membranosa la inmunoglobulina G tiende a estar por debajo del promedio de los normales con la excepción de un paciente (Fig. 1). Los niveles de inmunoglobulinas A y M se encontraron igual que en los normales, con excepción de un paciente que sobrepasó el promedio normal. Más del 50 por ciento del grupo de los pacientes con lesiones membrano-proliferativas tuvo niveles normales de inmunoglobulina G. Al comparar los membranosos con los membrano-proliferativos pudimos establecer una diferencia según los niveles de IgG, ya que todos menos uno de los membranosos se encontraban por debajo del promedio normal.

Las inmunoglobulinas G, A, y M aparecieron en las orinas de los pacientes con lesión membranosa (Fig. 2); mientras que en las orinas de aquellos con lesión membrano-proliferativa apareció solamente la IgG y la IgA, faltando la IgM.

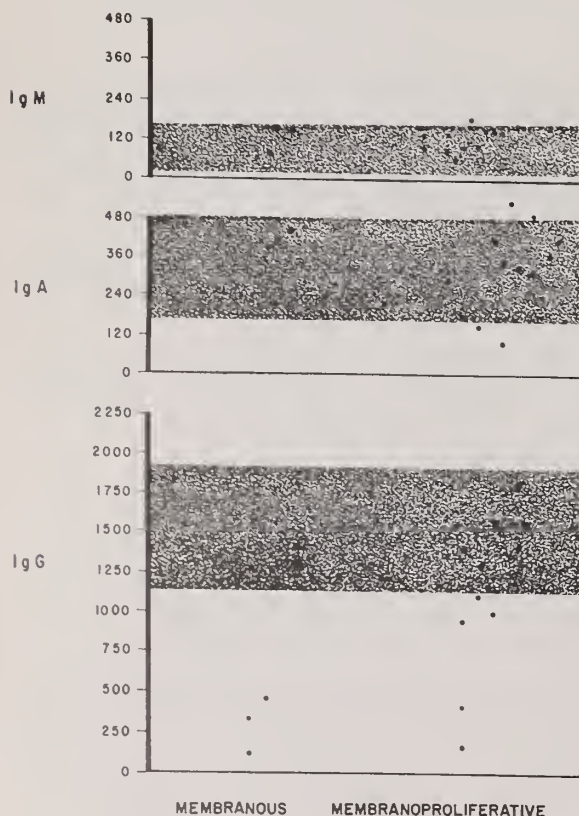


Fig. 1: Inmunoglobulinas séricas en el síndrome nefrótico del adulto.

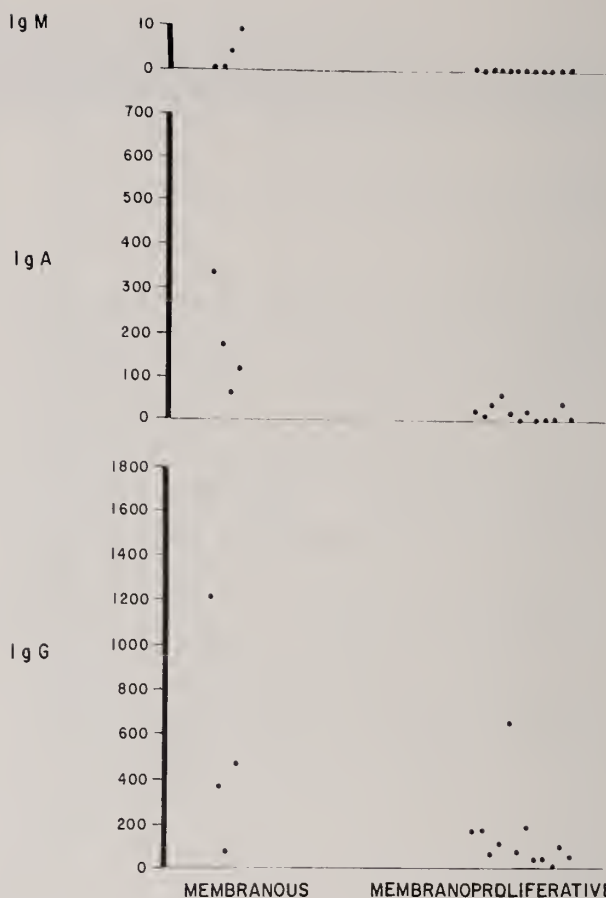


Fig. 2: Inmunoglobulinas de orina en el síndrome nefrótico del adulto.

La presencia de inmunoglobulinas en la orina depende, entre otras cosas, de los niveles en el plasma (9). Sin embargo los niveles plasmáticos pueden bajar sin que aparezcan inmunoglobulinas en la orina. Esto nos hace pensar que las inmunoglobulinas se están depositando en la membrana glomerular. Esta es la base para continuar nuestros estudios aplicando técnicas de inmunofluorescencia y microscopía electrónica en las biopsias de riñón.

La depuración de IgG, IgA, y IgM no fue significativamente diferente entre el grupo de lesiones membranosas y el de lesiones membrano-proliferativas (Fig. 3). Pero en ambos grupos se puede notar que la depuración de IgM fue baja.

La depuración de albumina, transferrina y macroglobulina alfa-2 se encontró aumentada tanto en los pacientes con lesiones membranosas como en aquellos con lesiones membrano-proliferativas (Fig. 4). Los niveles de macroglobulina alfa-2 se encontraron más altos en los membranosos que en las membrano-proliferativas. Un solo paciente con cambios membrano-proliferativos presentó niveles altos de macroglobulina alfa-2. Sin embargo los pacientes con lesiones membranosas poseían una

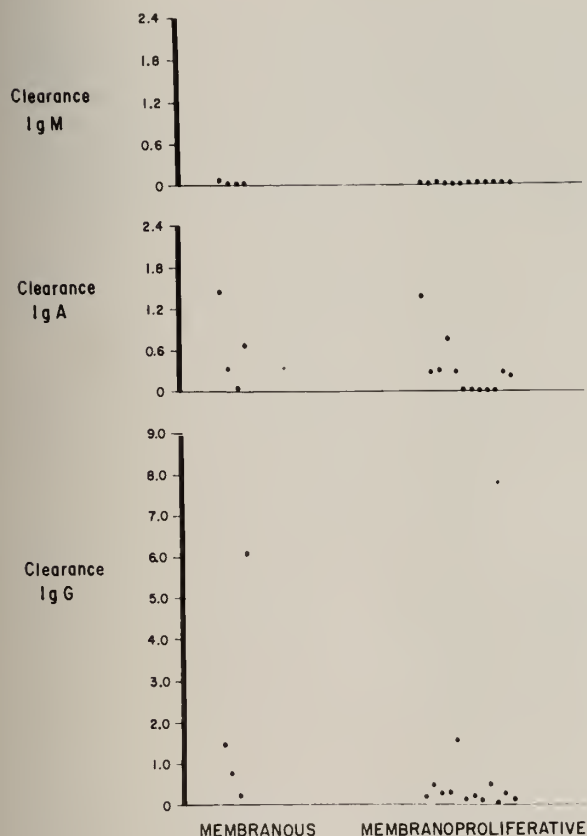


Fig. 3: Depuración de inmunoglobulinas en el síndrome nefrótico del adulto.

depuración de transferrina y albúmina mayor que los que padecían de lesión membrano-proliferativa (Fig. 4). Un número mayor de pacientes con lesiones membranosas nos permitirá documentar esta diferencia. La Fig. 5 muestra la falta de depuración de IgG, IgA y IgM en pacientes con riñón poliquístico y pielonefritis en contra-posición de aquellos con síndrome nefrótico en los cuales la depuración de inmunoglobulinas G y A están aumentadas. La Fig. 6 muestra el alto grado de selectividad de los pacientes con síndromes tubulares, riñón poliquístico y pielonefritis crónica quienes depuraron casi exclusivamente transferrina y albúmina, proteínas de bajo peso molecular (4, 5, 10).

Discusión

Nuestro estudio demostró que existe una relación entre el patrón de selectividad excretoria de proteínas y ciertas enfermedades renales lo cual nos ayuda a identificar el tipo de lesión, o sea, si esta es de origen tubular, o glomerular.

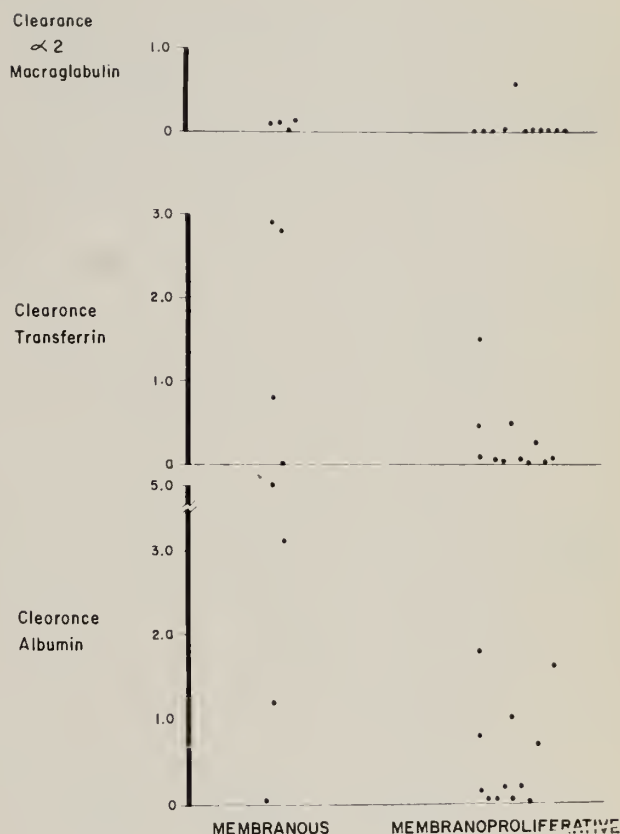


Fig. 4: Depuración de proteínas de bajo peso molecular en el síndrome nefrótico del adulto.

La depuración de albúmina o transferrina en ausencia de una depuración de inmunoglobulinas sugiere fuertemente una lesión tubular, que comprueba los hallazgos de Dillard *et al* (10) que una depuración alta de IgG, IgA y IgM sugiere la presencia de una lesión glomerular de tipo membranoso o membrano-proliferativa. El patrón de depuración de proteínas no permitió establecer una diferencia entre las lesiones glomerulares de tipo membranosas o las de tipo membrano-proliferativa. Sin embargo, aunque no es estadísticamente significativo, podemos ver una tendencia a una menor selectividad en las lesiones membranosas.

Resumen

La depuración de 6 proteínas fueron estudiadas en 26 pacientes renales, 16 de los cuales padecían de un síndrome nefrótico documentado por biopsia percutánea, mientras que 10 pacientes presentaron lesiones de tipo preponderantemente tubular (pielonefritis cró-

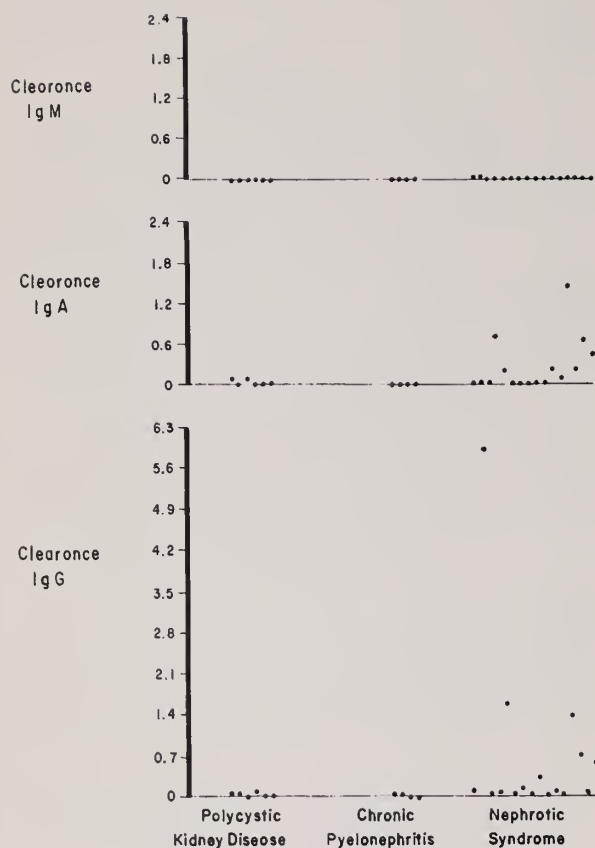


Fig. 5: Depuración de inmunoglobulinas en enfermedad renal adulta.

nica y riñón poliquístico).

Los pacientes con lesiones primordialmente glomerulares fueron sub-divididos en un grupo con lesiones membranosas y otro con lesiones membrano-proliferativas. Las depuraciones de albúmina, transferrina, IgG y IgA fueron altas en las lesiones glomerulares, con una tendencia a estar más elevada en el grupo membranoso.

Los pacientes con lesiones tubulares presentaron un alto grado de selectividad depurando casi exclusivamente transferrina y albúmina, proteínas de peso molecular bajo.

Summary

The renal clearance of 6 proteins was examined in 27 patients with renal disease. Sixteen patients had primary glomerular involvement as demonstrated by percutaneous renal biopsy while ten patients had tubular involvement (chronic pyelonephritis and polycystic kidney disease).

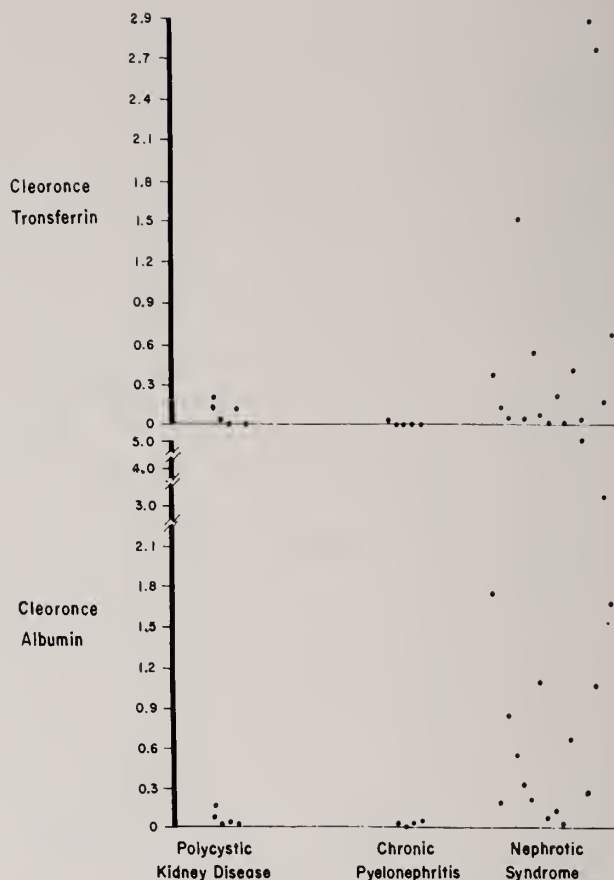


Fig. 6: Depuración de proteínas de bajo peso molecular en enfermedad renal adulta.

The patients with primary glomerular involvement were divided into two groups: membranous and membrano-proliferative. The clearances of albumin, transferrin, IgG and IgA were higher in the glomerular lesions. Those patients with primary tubular involvement showed a high degree of selectivity, namely on clearances of albumin and transferrin.

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PRUEBA DE EXCRESION URINARIA DE XILOSA: UTILIDAD Y LIMITACIONES EN LA SEPARACION DE NIÑOS NORMALES DE PACIENTES CON ESPRU TROPICAL

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La excreción en la orina de xilosa después de la ingestión oral de esta pentosa, en personas no edematosas y con función urinaria normal, refleja cambios en la absorción en el intestino delgado lo suficientemente bien para servir como una prueba de cernimiento muy confiable en la identificación de síndromes de malabsorción (1, 2, 3).

Fourman (4) en 1948 fue el primero que describió el uso de la prueba de absorción de D-xilosa en esteatorrea. Luego, Gardner y Pérez-Santiago (5) evaluaron la absorción de esta pentosa en esprü tropical. Originalmente se administraba una dosis oral de 25 gm, se determinaban los niveles sanguíneos cada hora y se medía la excreción urinaria durante un período de 5 horas. La excreción en la orina demostró ser más confiable que los niveles sanguíneos como indicador del grado de absorción intestinal de xilosa (5).

Butterworth y col. (2) en 1959 demostraron que la prueba con una dosis de 5 gm daba resultados tan confiables y reproducibles como con la dosis de 25 gm, con la ventaja de menor costo y ausencia de la intolerancia intestinal que ocasionalmente se observa con la dosis alta. En 1961 Santini y col. (6) confirmaron la confiabilidad de la prueba modificada en la separación de pacientes con esprü tropical de adultos normales.

El valor de la prueba de xilosa en la evaluación de malabsorción intestinal en niños ha sido discutido por varios autores (7, 8, 9). Pero el número de niños estudiado para establecer valores normales ha sido casi siempre pequeño. En 1971 nosotros publicamos datos sobre la absorción de xilosa en un grupo grande de niños normales y en otro grupo de niños con esprü tropical (10). El estudio de un grupo más grande de

pacientes de esprü durante el último año y medio nos ha permitido interpretar mejor los datos publicados previamente y nos ha revelado con mayor claridad la utilidad y limitaciones de la prueba de excreción urinaria de xilosa en niños. El propósito de esta publicación es presentarles nuestra experiencia con esta prueba.

Materiales y Métodos

Se determinó la excreción urinaria de D-xilosa, después de la ingestión de una dosis de 5 gm de esta pentosa, en tres grupos de niños: 1) 158 sujetos normales (grupo control), 2) 51 niños con esprü tropical antes de tratamiento, y 3) 31 pacientes de esprü tropical ya tratados. La D-xilosa, "reagent grade", se disolvió en 100 a 120 ml de agua en vasos de papel y se administró oralmente a los niños en ayunas. Los vasos se lavaron con 150 ml adicionales de agua, los cuales se tomaron, para asegurar la ingestión completa de la dosis. Luego, los sujetos tomaron agua ad lib cada 1 o 2 horas para asegurar una excreción urinaria adecuada (más de 200 ml/M²). Se recogió toda la orina pasada durante el período de 5 horas después de ingestión de la xilosa. El contenido de xilosa en la orina se determinó en 24 a 48 horas por el método de Roe y Rice (11).

El grupo control consistió de 160 niños que asistían al "nursery, kindergarten", primero, segundo y cuarto grados en una escuela pública de San Juan, Puerto Rico. Todos los niños estudiados procedían de familias de ingresos bajos. A todos se les tomó un historial médico, incluyendo información sobre su estado nutricional, con la ayuda de sus padres. Los autores examinaron a cada niño con atención particular a síntomas y signos sugestivos de malabsorción intestinal. A los sujetos que demostraron palidez al examen se les determinó la concentración de hemoglobina, y se les hizo examen de un extendido de sangre.

El diagnóstico de esprü tropical en los pacientes estudiados se basó en la presencia de: 1) historial de anorexia, pérdida de peso, diarrea crónica y glositis, 2) eritropoiesis megaloblástica, 3) anomalías compatibles con esprü tropical en la biopsia de mucosa de yeyuno y 4) respuesta buena a tratamiento para esprü tropical (12, 13). Nueve pacientes a quienes se les hizo la prueba de absorción de vitamina A tuvieron una curva anormal. La concentración sérica de folato y vitamina B₁₂ fue bajo lo normal en la mitad de los pacientes que se examinaron. La terapia de los pacientes de esprü tropical incluyó ácido fólico, vitamina B₁₂, sulfasuxidina o tetraciclina, en varias combinaciones, por 6 meses a 2 años. Todos estos pacientes estuvieron asintomáticos o mejorados clínicamente y muchos demostraron mejoría en la mucosa del yeyuno después de la terapia.

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TABLA I: EXCRECION URINARIA DE XILOSA EN NIÑOS DURANTE LAS PRIMERAS CINCO HORAS DESPUES DE INGERIR DOSIS ORAL DE 5 GM

Grupo	No. Casos	Rango gm	Promedio gm	Desviación Standard (DS) gm	Rango de Promedio ± 2 D S gm
Control	158	0.7 - 2.3	1.44	± 0.35	0.7 - 2.1
Esprrú sin tratar	51	0.2 - 1.4	0.59	± 0.27	0.1 - 1.1
Esprrú tratado	31	0.6 - 2.3	1.44	± 0.46	0.5 - 2.4

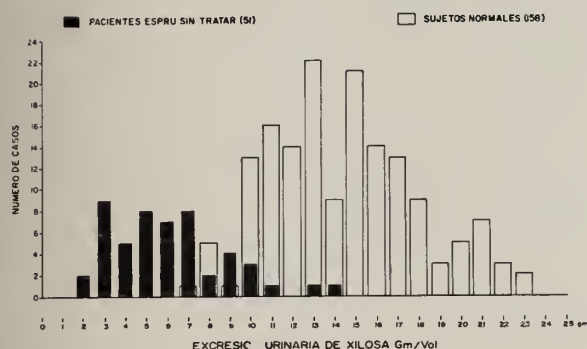


Fig. 1: Curva de distribución de excreción urinaria de xilosa en 5 horas, después de ingerir dosis de 5 gm oralmente, en niños normales y en pacientes con esprrú tropical sin tratarse.

Resultados

Ciento ochenta y ocho sujetos, 89 varones y 69 hembras, se consideraron adecuados para incluirse en el grupo control. Sus edades variaron de 2 1/2 a 13 años, con promedio de 6.6. Dos niños fueron descartados del grupo original de 160; a uno que tuvo una excreción de xilosa de 0.5 gm se le había diagnosticado esprrú tropical recientemente en un hospital local y otro, quien tuvo una xilosa de 0.3 gm, tenía algunos síntomas sugestivos de malabsorción y la biopsia intestinal demostró una mucosa anormal.

La excreción urinaria de xilosa en el grupo control varió de 0.7 a 2.3 gm (14 por ciento a 46 por ciento de la dosis oral) con un promedio de 1.44 gm (29 por ciento) y desviación standard de ± 0.35 gm. La distribución de los valores de excreción de xilosa en niños por edades ha sido presentada en una gráfica de otra publicación (10).

El grupo de pacientes con esprrú tropical sin tratar incluyó 51 niños cuyas edades fluctuaron entre 2 y 16 años. La excreción de xilosa en la orina en esos pacientes varió de 0.2 a 1.4 gm, con promedio de 0.59

(12 por ciento) y desviación standard de ± 0.27 gm. En 31 pacientes tratados para esprrú tropical por 6 a 24 meses la excreción fue de 0.6 a 2.3 gm con media de 1.44 y desviación standard de ± 0.46 gm.

La Tabla 1 compara los valores de excreción urinaria de xilosa en los varios grupos estudiados. La figura 1 presenta la distribución de valores en los niños normales y en los pacientes de esprrú tropical antes de recibir tratamiento.

Catorce niños en el grupo control demostraron palidez al examen, pero su hemoglobina varió de 11.6 a 14.4 gm/100 ml, con promedio de 12.9. Ninguno de ellos tuvo macrocitosis ni ningún otro signo de deficiencia de ácido fólico y/o vitamina B₁₂. Hubo 13 niños con anorexia marcada y/o bajo peso para su edad, distensión abdominal y glositis leve. Uno de ellos tuvo una hemoglobina de 9.6 gm/100 ml con hipocromia y microcitosis en el extendido de sangre. Su excreción de xilosa fue de 1.1 gm. La hemoglobina en los otros 12 niños varió de 11.6 a 13.4 gm/100 ml, y la excreción de xilosa fluctuó de 0.8 a 2.2 gm, con promedio de 1.48 gm. Sólo 4 de los 158 sujetos en el grupo control presentaron peso por debajo de la tercera percentila, y sólo 2 tuvieron estatura por debajo de la percentila tercera cuando se compararon con niños normales de Puerto Rico y de Estados Unidos de América (14, 15).

Discusión

La excreción urinaria de xilosa en nuestros 158 sujetos normales varió de 0.7 a 2.3 gm (10). Siete casos (4.4 por ciento) de ellos excretaron menos de 1.0 gm (20 por ciento de la dosis ingerida). Pero el límite inferior de excreción, con 95 por ciento de confiabilidad (promedio menos 2 desviaciones standard) fue 0.74 gm. Es de interés notar que todos excepto uno de los 7 niños que eliminaron 0.9 gm o menos en el grupo control fueron niños de 6 o menos años de edad. Mas aún, el rango del promedio ± 2 desviaciones standard de excreción urinaria de xilosa en niños de 6 1/2 a 13 años

de edad (65 niños) es 0.9 a 2.1 gm, cuyo valor inferior es bastante más alto que el del grupo de niños más jóvenes (0.7 gm), aunque la diferencia no es estadísticamente significativa. Estos hallazgos en nuestros pacientes y otras publicaciones sugieren que los niños pequeños normalmente tienen una absorción menor de xilosa que los mayores (16, 17).

La distribución de valores de excreción urinaria de xilosa en los pacientes de espú no tratados fue relativamente amplia, según se puede apreciar en la figura 1, variando de 0.2 hasta 1.4 gm, con promedio 0.59 y desviación standard de ± 0.27 gm. Por lo tanto, el límite superior de excreción de xilosa en estos pacientes (con 95 por ciento de confiabilidad) es de 1.1 gm, valor que con bastante frecuencia puede encontrarse en niños normales. La superposición parcial de las curvas de distribución de las dos poblaciones no permite separar con certeza los niños normales de los pacientes de espú que se presentan con excreción urinaria de xilosa en el rango de 0.7 a 1.4 gm. Sin embargo para todos los efectos prácticos se puede asumir que cualquier valor de menos de 1.0 gm en niños mayores de 3 años es anormal y que valores entre 1.0 y 1.2 son dudosos. Es importante recordar que aunque un valor de excreción urinaria de xilosa de más de 1.1 gm hay que considerarlo normal (por probabilidades estadísticas), ocasionalmente puede haber pacientes de espú tropical con valores sobre esa cantidad. Dos de 51 pacientes (4 por ciento) en nuestra serie tuvieron 1.3 y 1.4 gm, respectivamente, aunque tenían otros criterios que justificaban establecer el diagnóstico de espú tropical.

En cinco pacientes de enfermedad celiaca estudiados por Clark (6) en 1962 la excreción urinaria de esta pentosa fue de menos de 15 por ciento. Hubble y Littlejohn (8) en 1963 encontraron una excreción urinaria de xilosa de menos de 0.75 gm (15 por ciento de la dosis administrada) en 6 de 7 pacientes de enfermedad celiaca antes de tratarse. En el otro paciente, la excreción de la pentosa fue 24 por ciento (1.2 gm) a pesar de la presencia de esteatorrea considerable y de cambios severos en el intestino delgado demostrables en examen radiológico e histológico.

Casi todos los pacientes con espú tropical tratados y re-examinados por nosotros demostraron una pronta mejoría en la excreción de xilosa, la mayor parte de ellos alcanzando valores normales en pocos meses. El promedio y la desviación standard en este grupo son muy similares a los del grupo control. Sin embargo los valores de 6 de 31 casos (16.0 por ciento) permanecieron por debajo de 1.0 gm, en comparación con 7 de 158 (4.4 por ciento) del grupo de niños normales, lo que sugiere

que algunos de estos pacientes no habían recobrado de su malabsorción de xilosa.

Estos datos sobre la excreción urinaria de xilosa nos demuestran que esta prueba es menos confiable en niños que en adultos en la separación de sujetos normales de pacientes de espú tropical (4, 5). Apparently esta dificultad también ocurre en el diagnóstico de niños con enfermedad celiaca según se desprende de la data de Hubble y Littlejohn a que hicimos referencia anteriormente.

Nuestro estudio confirma que la excreción de xilosa usando una dosis de 5 gm es una prueba sencilla y confiable para evaluar la absorción intestinal. Esta es una prueba muy útil para el cernimiento de pacientes pediátricos con espú tropical y para su seguimiento una vez tratados. Sin embargo, la prueba es menos confiable en niños que en adultos para separar niños normales de otros con espú.

Resumen

La prueba de excreción urinaria de xilosa durante 5 horas, después de la administración oral de 5 gm de esta pentosa, se realizó en 158 niños normales de Puerto Rico de 2 1/2 a 13 años de edad. Los valores fluctuaron entre 0.7 a 2.3 gm, con un promedio de 1.44 y desviación standard de ± 0.35 gm. Siete niños (4.4 por ciento) excretaron menos de 1 gm (20 por ciento de la dosis ingerida), y todos ellos, excepto uno, fueron sujetos menores de 6 1/2 años.

Cincuenta y un niños enfermos con espú tropical examinados con esta prueba demostraron valores entre 0.2 y 1.4 gm, con promedio de 0.59 y desviación standard de 0.27. El límite superior de excreción de xilosa en estos pacientes (con 95 por ciento de confiabilidad) es de 1.1 gm, valor que con bastante frecuencia puede encontrarse en niños normales. Para todos los efectos prácticos, podemos asumir que cualquier valor de menos de 1.0 gm es anormal y que valores entre 1.1 y 1.2 gm son dudosos.

Treinta y un pacientes de espú tratados demostraron una excreción urinaria de xilosa entre 0.6 y 2.3 gm con promedio de 1.44 y desviación standard de 0.46 gm, valores que son muy similares a la del grupo control.

Nuestro estudio confirma que la prueba de excreción urinaria de xilosa, usando una dosis de 5 gm, es sencilla y confiable para evaluar pacientes en quienes se sospecha espú tropical. También es útil para el seguimiento de estos pacientes una vez tratados. Sin embargo, la prueba es menos confiable en niños que en adultos para separar niños normales de otros con espú.

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DISCURSO

LA PROFESION MEDICA ANTE LOS CAMBIOS QUE SE AVECINAN

Félix S. Vidella Suau, MD

Hemos llegado una vez más al final de otro año de gestión presidencial en nuestra Asociación Médica, durante el cual he tenido el privilegio y el honor de dirigir los destinos de nuestra prestigiosa institución.

En este año se han realizado múltiples actividades y se han tenido que adoptar posiciones verdaderamente verticales, a expensas de no ser comprendidos, y aún de ser criticados, pero estamos tranquilos y satisfechos ya que las posiciones adoptadas y las resoluciones tomadas, han sido hechas teniendo en mente la salud y el bienestar de todos nuestros conciudadanos, especialmente, de aquellos de escasos recursos económicos, a fin de que reciban la mejor calidad de servicios de salud disponibles en nuestra comunidad.

Si bien, como antes señaláramos, este año ha sido uno lleno de retos y alternativas, auguro que los próximos serán aún más difíciles y decisivos para el futuro de la medicina. Ante esta situación tenemos la imperiosa necesidad de estar fuertemente unidos, y que una sola voz se deje oír a través de todo Puerto Rico. Si queremos que el derecho de nuestros pacientes a recibir el mejor cuidado médico posible sea protegido, que no se interfiera con el tratamiento individual que requieren nuestros pacientes, y que la opinión de los médicos puertorriqueños sea escuchada, la sola voz que se debe oír debe ser la voz de nuestra Asociación Médica.

La Asociación Médica de Puerto Rico, como representante de la medicina organizada, ha asumido dicha responsabilidad, sirviendo como intermediaria entre el Gobierno y la profesión médica.

Es nuestra opinión que la iniciativa privada puede obtener, y de una manera más efectiva, el mejor ambiente y la expansión de los servicios de salud que nuestros conciudadanos necesitan y se merecen. Sin embargo, en sectores donde la iniciativa privada no posee los recursos necesarios, hemos recomendado y

respaldado diversos programas gubernamentales.

Por otro lado, no creemos que se le deba permitir al Gobierno que dicte pautas de cómo y en qué forma se debe practicar la medicina, y que a la vez tenga la exclusividad en la enseñanza de nuestra profesión. Esas decisiones deben estar en manos de quienes, por sus conocimientos, experiencia y buen juicio están entrenados y capacitados para ejecutarlas, esas decisiones deben estar en manos de la profesión médica. Por eso, es nuestra opinión que el Gobierno debe ser un agente acrecentador y catalítico y no un agente controlador.

Y todo esto aplica al seguro médico universal que se avecina, y que en mi opinión, es necesario para la salud y el bienestar de todo nuestro pueblo. Cualquier seguro médico que eventualmente se apruebe, debe permitir al médico practicar la medicina de la manera que él crea correcta, pero estableciendo la fiscalización que fuese necesaria de parte de sus propios compañeros de profesión. Igualmente, al paciente se le debe garantizar el derecho a escoger libremente el proveedor de servicios de salud, así como el de cambiar de proveedor según su deseo.

Hay actualmente ante el Senado de Puerto Rico un Proyecto de Ley que, de aprobarse, nacionalizaría todos los servicios de salud en nuestra Isla, y el que estamos convencidos, será detrimental para la salud de nuestros pacientes. No ofrece libre selección, interfiere con la responsabilidad que tenemos en el cuidado del paciente, establece un verdadero monstruo burocrático y por consiguiente, una definitiva escasez de fondos con sus consabidas y trágicas consecuencias.

Estamos plenamente convencidos que se impone un cambio, que nuestro sistema de salud requiere ciertas modificaciones y mejoras. Pero a la vez, no creemos necesario ni prudente un cambio total en el sistema, como lo proponen unos pocos, y menos aún creemos en la implementación de sistemas de otros países, ya que a pesar de múltiples deficiencias, el nuestro ha obtenido grandes logros a través de los años. Lo que se haga debe hacerse de acuerdo con nuestras necesidades, con nuestras realidades económicas y sociales y nuestra idiosincracia puertorriqueña.

Discurso presidencial durante la Sesión Inaugural de la Setuagésima Asamblea Anual de la Asociación Médica de Puerto Rico, celebrada en el Hotel San Juan el 15 de noviembre de 1972.

Este es el reto que tenemos en nuestras manos, y la Asociación Médica de Puerto Rico ofrece aquí, hoy, como lo ha hecho en múltiples ocasiones anteriores, sus conocimientos y experiencia en pro de lograr un seguro médico abarcador para todos los puertorriqueños, que garantice no sólo su salud y bienestar, sino también su libertad.

Compañeros, para finalizar, deseo repetir lo que expresé en mi discurso de Toma de Posesión: "La Asociación Médica de Puerto Rico está en actitud de ampliar sus derroteros, con el fin de cumplir a cabalidad con sus objetivos. La única forma en que podemos responder a los grandes retos que tenemos

por delante, es adelantándonos a los tiempos en que vivimos, no vivir a la zaga. Tenemos que vivir en el mañana, buscar nuevos caminos, cultivar la insatisfacción creadora, romper con los tradicionalismos. Vivimos en un mundo que busca nuevas formas de afirmación de la libertad y la democracia. A nosotros nos toca el gran deber de afirmar el ejercicio de una medicina de excelencia, en un mundo de democracia y de libertad en todos los planes y sin limitaciones. La profesión médica puede y debe tener sus controles y reglamentaciones, pero hay que ejercerla en libertad".

EDITORIAL

ACCION Y REFLEXION

Todo profesional, así como toda agrupación de profesionales, tiene la obligación moral de servir a su país, a su comunidad y a sus conciudadanos.

La Asociación Médica de Puerto Rico, representante de la medicina organizada, desde su fundación ha mantenido un limpio historial de servicio a los puertorriqueños.

Con el propósito de servir a la comunidad puertorriqueña, la Asociación Médica se ha enfrentado y opuesto a decisiones mal hechas y programas de salud mal establecidos. Esta labor de la Asociación Médica ha sido mal interpretada en algunas ocasiones, con o sin intención, en forma adversa ante la opinión pública. Pero, tenemos el firme propósito de continuar nuestra labor, y la Asociación Médica de Puerto Rico participará en el desarrollo diario de la vida puertorriqueña como una unidad integrada, conjuntamente con otras agrupaciones y con la comunidad a la que sirve y quiere seguir sirviendo.

Primero, la Asociación Médica ha sostenido, sostiene y sostendrá el derecho que tiene todo individuo a la salud. Para asegurar el disfrute de este derecho en el más amplio sentido de la palabra, todo individuo debe tener a su disposición el mejor cuidado médico y la más alta calidad de medicina irrespectivo de su raza, color, sexo, condición económica, religión, y muy importante, su afiliación política. La salud del pueblo no debe utilizarse, ni permitiremos que se utilice, como un medio para hacer capital político. La salud, como indiqué, es un derecho, y los derechos no se discuten, se reconocen. La Asociación Médica se compromete a mantener la calidad de los servicios médicos.

Es de sumo interés profesional cómo los puertorriqueños insatisfechos con los servicios que actualmente se les rinden, claman por un cambio; claman por obtener mejores servicios. La salud es la espina dorsal de un pueblo. Para mantener la salud, se debe ajustar uno a las necesidades y realidades del presente con una proyección al futuro. Aunar los esfuerzos de todos los sectores de nuestra comunidad, es necesario para esto, a fin de lograr un objetivo común, y este objetivo debe ser el bienestar de los puertorriqueños.

La prestación de los servicios de salud no debe, ni puede ser prerrogativa exclusiva de un sector, bien sea gubernamental o privado. El resultado de pretender prestar servicios de salud como prerrogativa exclusiva de un sector de la comunidad, lo hemos palpado ya aquí en Puerto Rico: malos servicios a un costo ridículamente alto para el erario público, cuando con mejor planificación pudo haberse obtenido servicios mejores y más baratos mediante el uso de facilidades privadas.

La aplicación inadecuada de la Ley de la Integración de la Medicina, la ley 56, ha causado un desplazamiento de personas insolventes de los hospitales del Gobierno por personas económicamente pudientes.

Segundo, debe existir una planificación completa y realista de la salud en Puerto Rico, a tono con las realidades del sistema económico y político que el pueblo de Puerto Rico ha escogido. Es necesario considerar por igual las partes que componen el conglomerado responsable de prestar los servicios, con justicia e igualdad, y es nuestra obligación moral no permitir un plan que beneficie a unos en perjuicio de otros.

Tercero, los fondos destinados a la salud del pueblo deberán utilizarse para obtener en la forma más rápida y mejor posible, la mejor salud para todos. Se ha hablado de la integración de los sistemas de prestación de servicios médicos, pero lo que se ha hecho es una desintegración de esos servicios en perjuicio de los pacientes. Los fondos públicos han sido canalizados para la construcción de unidades hospitalarias cada vez más costosas y complejas en su funcionamiento sin considerar darle uso máximo a las estructuras existentes, ya sean públicas o privadas, cada día más accesibles a todos por nuestra limitada geografía y el progreso de nuestros métodos de transportación.

El éxito obtenido, si alguno, de los programas de salud en Puerto Rico se debe en su mayor parte a la generosidad profesional y al espíritu de servicio de los médicos puertorriqueños y de las instituciones que prestan servicios de salud. Se ha pretendido, y temo que ha sido logrado, causar la impresión de que los médicos y las instituciones, se enriquecen a costa del pueblo. Salvo raras excepciones, es de todos conocidos los bajos honorarios que reciben los médicos de los planes de seguro gubernamentales y privados. Es una realidad, que ningún sistema de salud que dependa de la generosidad de los médicos podrá perdurar, y mucho menos conseguir buenos y eficientes servicios para el pueblo, ya que consideramos debe tratarse a los médicos, que son los trabajadores de la salud, con los mismos principios de justicia con que merecen ser tratados los pacientes.

La calidad de los servicios de salud a que todo individuo tiene derecho, no debe depender del sitio o institución a que tenga acceso por razones económicas. Todos los servicios, bien sean prestados por agencias gubernamentales o entidades privadas, deben ser de la mejor calidad.

Por esta razón tienen que producirse cambios fundamentales en la estructuración de los sistemas de salud y esta re-estructuración conlleva un esfuerzo real y efectivo por parte de los médicos y demás componentes del equipo de la salud con objeto de que se haga una buena y eficiente prestación de los servicios. A estos fines, lucharemos para que se establezca en todos los hospitales de Puerto Rico un Comité de Utilización. Estos Comités deben ser operados y deberán estar provistos de la autoridad necesaria para salvaguardar la calidad de la medicina practicada.

Aquellas instituciones de salud a quienes por legislación se ha concedido una exención contributiva y son receptores de fondos gubernamentales, deben retribuir con una mayor cantidad de servicios hospitalarios a personas menos afortunadas. La prestación de los mismos es una condición esencial para la obtención de la exención contributiva, y debe por tanto, cumplirse con esta responsabilidad. Considero necesario que en beneficio de los ciudadanos se exija por parte de la correspondiente agencia gubernamental el fiel cumplimiento de esta condición.

La Asociación Médica respaldó y respaldará el establecimiento de seguros médicos abarcadores, que cubran a toda la población de nuestra Isla. Sin embargo, éstos tienen que incluir los servicios básicos de una medicina integral: libre selección de médico y hospital, en toda la extensión del concepto, sin ataduras o reglamentación: derecho para escoger libremente al médico de su confianza y sin limitaciones; con igualdad y justicia. Bajo ningún concepto, deberá esbozarse un plan que beneficie a unos en perjuicio de otros.

Igualmente, es necesario e imprescindible que se implemente en toda su extensión el programa de libre selección de médico y hospital.

La sociedad puertorriqueña está profundamente preocupada por el problema social que causa la droga-adicción. Sobre ello se ha hablado mucho, tanto por personas que saben, y mucho más por las que no saben, pero considero necesario una mayor y más efectiva participación de los médicos en la implementación de los programas necesarios para la eliminación de este problema.

Es de todos conocida, la necesidad de una revisión del Código Penal. Exhortamos al Colegio de Abogados para que con la mayor urgencia promueva dicha revisión. La revisión del Código Penal deberá hacerse no sólo con el propósito de castigar al delincuente, sino que deberá aprovecharse de los avances de las ciencias que analizan la conducta de los individuos y lograr su rehabilitación. Tene-

mos los conocimientos y los ponemos a la disposición para ayudar en todo lo que sea necesario.

Considero a la Asociación Médica un guardián de la buena práctica de la medicina y por esta razón estaremos muy atentos a las quejas que se nos sometan referente a todo lo que en forma alguna afecte la buena y eficiente prestación de los servicios.

Existe la necesidad, sin embargo, de mantener la unión cordial, no importa las disparidades de criterio que en un momento dado puedan existir, y que estoy consciente, surgen con un propósito común, que es el de hacer lo que mejor se puede en beneficio de todos.

José M. Rigau, MD

NOTA BIOGRAFICA



DR. JOSE M. RIGAU MARQUES

Presidente, Asociación Médica de Puerto Rico

1972

Nació el Dr. José M. Rigau Marqués en Santurce, Puerto Rico, el 15 de octubre de 1925. Cursó sus estudios generales en el Colegio San José de Río Piedras, P. R. En el 1946 fue licenciado en ciencias en la Universidad de Tulane, Nueva Orleans, La., y se graduó de Doctor en Medicina de la Universidad Central de Madrid, España, en el 1955. Internó en el Hospital Municipal de Río Piedras, y completó su entrenamiento quirúrgico en el Hospital San Patricio de la Administración de Veteranos de San Juan. Ha trabajado como cirujano en el Hospital de la Administración de Veteranos, en el Hospital de Salud de Cayey, en el Hospital Ruiz Soler de Bayamón, en el Hospital San Carlos, y en el Hospital San Rafael de Caguas.

Es miembro de la Asociación Médica Americana, Asociación Puertorriqueña de Graduados Universidades Españolas, de la Sección de Cirugía de la AMPR, del Instituto Puertorriqueño de Cultura Hispánica y candidato al Colegio Americano de Cirujanos y al Colegio Americano de Chest Physicians.

Es miembro de la Asociación Médica de Puerto Rico desde el 1964 y ha participado en numerosos Comités y actividades de la Asociación.

ALL IN HIS HEAD:

• Watery Eyes

Nasal
Congestion

Sneezing

Runny Nose

**THE COLD
SYMPTOMS
THAT
MAKE HIM
MISERABLE**

ALL IN 'ORNADE:

Drying Agent
(isopropamide,
as the iodide—
2.5 mg.)

Decongestant
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amine HCl—50 mg.)

Antihistamine
(chlorpheniramine
maleate—8 mg.)

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INGREDIENTS
HE NEEDS
FOR PROLONGED
RELIEF**

Before prescribing, see complete prescribing information in SK&F literature or PDR.

Indications: Upper respiratory congestion and hypersecretion associated with: the common cold; acute and chronic sinusitis, vasomotor rhinitis; allergic rhinitis (hay fever, "rose fever," etc.).

Contraindications: Hypersensitivity to any component; concurrent MAO inhibitor therapy; severe hypertension; bronchial asthma; coronary artery disease; stenosing peptic ulcer; pyloroduodenal or bladder neck obstruction. Children under 6.

Warnings: Advise vehicle or machine operators of possible drowsiness. Warn patients of possible additive effects with alcohol and other CNS depressants.

Usage in Pregnancy: In pregnancy, nursing mothers and women who might bear children, weigh potential benefits against hazards. Inhibition of lactation may occur.

Effect on PBI Determination and I^{131} Uptake: Isopropamide iodide may alter PBI test results and will suppress I^{131} uptake. Substitute thyroid tests unaffected by exogenous iodides.

Precautions: Use cautiously in persons with cardiovascular disease, glaucoma, prostatic hypertrophy, hyperthyroidism.

Adverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth; nervousness; or insomnia. Also, nausea, vomiting, epigastric distress, diarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal pain, irritability, palpitation, headache, incoordination, tremor, dysuria, difficulty in urination, thrombocytopenia, leukopenia, convulsions, hypertension, hypotension, anorexia, constipation, visual disturbances, iodine toxicity (acne, parotitis).

Supplied: Bottles of 50 capsules.

SK&F Smith Kline & French Laboratories

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ORNADE® SPANSULE®

Each capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate); 50 mg. of phenylpropanolamine hydrochloride; 2.5 mg. of isopropamide, as the iodide.

brand of sustained release capsules

UNCOMMON RELIEF FOR COLD SYMPTOMS

If you've seen one, have you really seen them all?

The following patient profiles represent typical clinical situations, but do not necessarily represent actual cases.

Age 22, previously normal menses with occasional menorrhagia. Now on a sequential O.C. for four months. Complains of heavy flow, occasional intracyclic bleeding, edema, tender swollen breasts.
Indicates estrogen excess.
1st choice: Switch to a combination 50-mcg.-estrogen O.C. (such as **Demulen**[®]).

Age 19, small breasts, minor hirsutism, oily hair and skin. History of metrorrhagia, skipped or scanty menses. New user.

Indicates androgenic excess or estrogen deficiency (fertility is suspect).

1st choice: An estrogen-dominant O.C. (such as **Enovid-E**[®]).

Age 25, average frame, poor complexion. No problem with menses, normal para 1. On a low-estrogen/high-progestogen O.C. for two years. Now complains of scanty flow, decreased libido, depression.

Indicates probable buildup of progestogen-related side effects.

1st choice: Switch to a center-spectrum O.C. with more estrogen, less progestational activity (such as **Ovulen**[®]).

Age 21, short, mammosome, with normal menses, some acne. Was put on pre-nuptial regimen of 50-mcg.-estrogen/moderate-progestogen O.C. for two months. Now has increased acne.

Indicates metabolic production of androgen or relative estrogen deficiency.

1st choice: Switch to a 100-mcg.-estrogen combination (such as **Enovid-E**[®] or a sequential).



Unmasked, physiologically and anatomically, they're not all the same. A basic difference lies in their hormone profiles. One may secrete too much estrogen, another not enough...or perhaps too much androgen; the vast majority would fit somewhere into the broad center spectrum.

Although the profiles described below may not be completely predictive, in optimal O.C. selection, the estrogen-progestogen activity ratio should be carefully matched to the patient profile. Searle offers you O.C.s in a range not only suitable for your patients in the balanced center spectrum, but also adaptable to the patient with another type of hormone profile.

Oral contraceptives are complex medications. Among the commonly reported adverse reactions are: intracycle bleeding, fluid retention, tender or swollen breasts, exacerbation of acne condition, changes in libido, amenorrhea while on medication and upon discontinuance, nausea, leg cramps, headaches, weight gain. Therefore, after reference to the prescribing information, oral contraceptives should be prescribed with care.

*Note: In some patients any level of exogenous estrogen or progestogen may produce symptoms of excess hormone activity.

Age 25, tall, slender, athletic, with flat chest. On a progestogen-dominant 50-mcg -estrogen O.C. Has recurrent trichomoniasis and Monilia.

Indicates estrogen deficiency and excess of progestogen in current O.C.

1st choice: Switch to a combination pill with 100 mcg estrogen and less progestational activity (such as **Enovid-E**[®] or **Ovulen**[®] or a sequential).

Age 23, "Miss America" figure, previously normal menses, healthy skin and hair. On a 50-mcg -estrogen pill for four months. Complains of intracyclic bleeding.

Indicates probable need for more estrogen.

1st choice: Switch to a center-spectrum O.C. with more estrogen and moderate progestogen dominance (such as **Ovulen**[®]).

Age 21, college senior, average build. On highly progestogen-dominant/low-dose-estrogen O.C. for six months. Now complains of amenorrhea, between-cycle headaches, weight gain.

Indicates probable progestogen excess.

1st choice: Switch to a center-spectrum pill (such as **Ovulen**[®]).

Age 27, slightly overweight, multiparous. Nausea with all three pregnancies and with a sequential O.C. three years ago. Has premenstrual fluid retention and leg cramps.

Indicates probable excess of estrogen.

1st choice: A 50-mcg -estrogen/progestogen-dominant pill (such as **Demulen**[®]).

Ovulen[®] a balanced center-spectrum O.C. for most

Each white tablet contains ethynodiol diacetate 1 mg./mestranol 0.1 mg.

Demulen[®] a moderately progestogen-dominant O.C. for many

Each white tablet contains ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg.

Each pink tablet in Ovulen-28[®] and Demulen-28[®] is a placebo, containing no active ingredients. Both Ovulen and Demulen are available in 21- and 28-pill schedules.

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Enovid-E[®] a moderately estrogen-dominant O.C. for some

Each tablet contains norethynodrel 2.5 mg./ mestranol 0.1 mg.

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Where "The Pill" Began

For a brief summary of prescribing information, please see next page.

a family of O.C. products to help you match
the right pill to the right patient

Ovulen®

Each white tablet contains
ethynodiol diacetate 1 mg/mestranol 0.1 mg.

Demulen®

Each white tablet contains
ethynodiol diacetate 1 mg/ethinyl estradiol 50 mcg.

Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.

Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain^{1,2} leading to this conclusion, and one³ in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll¹ was about sevenfold, while Sartwell and associates⁴ in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations pre-existing uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and

the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function; increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T₃ uptake values; metyrapone test and pregnanediol determination.

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norethynodrel 2.5 mg/mestranol 0.1 mg

Actions—Enovid-E acts to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Enovid-E depresses the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Indication—Enovid-E is indicated for oral contraception.

The **Special Note, Contraindications, Warnings, Precautions and Adverse Reactions** listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

Enovid-E®

brand of norethynodrel with mestranol

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Where "The Pill" Began

BOLETIN

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ENERO A DICIEMBRE DE 1972

NUMS. 1-12

Enero:

Acute Oliguric Renal Failure Associated with Low-Molecular-Weight Dextran	1
<i>Rafael Burgos Calderón and Julio E. Figueroa</i>	
Treatment of Schistosomiasis Mansoni in Adults with Sodium Dimethylcysteine Tartrate	5
<i>Federico Hernández Morales and José Oliver González</i>	
Impresiones Dermopapilares: Dermatoglíficos y Surcos de Flexion. I. Conceptos Básicos	8
<i>Adolfo Pérez Comas and José Miguel García Castro</i>	
Editorial: Dextran 40 - Paradox of Treatment	14
<i>José L. Cangiano</i>	
Noticias	15

Febrero:

Tetralogía de Fallot: Conceptos Actuales de su Tratamiento	17
<i>Rafael Villavicencio, Jorge Sánchez y Amalia Martínez Picó</i>	
Constricción Quirúrgica de la Arteria Pulmonar: Experiencia en 80 Casos	23
<i>Agustín Muñoz, Edda Torres de Arraut y Amalia Martínez Picó</i>	
Marcapasos en Niños: Diez Años de Experiencia Clínica	31
<i>Mercedes Vega Vidal</i>	
Editoriales: Cardiología Pediátrica: Alcances en Puerto Rico	39
<i>Amalia Martínez Picó</i>	
Ejemplo, Problemas y Preguntas	
<i>Jorge O. Just Viera</i>	
Noticias	41

Marzo:

Nueva Operación Para Atresia Tricuspídea, Pulmonar y Condiciones Asociadas con Malformación del Ventrículo Derecho. I. Aspectos Quirúrgicos	44
<i>Jorge O. Just Viera, Ernesto Rivé Mora y Olga Rodríguez</i>	
Immunosuppressive Therapy - Basic Concepts and Recent Advances	48
<i>Julio E. Lergier</i>	

Human Macellaria Myiasis in Puerto Rico	53
<i>Irving Fox and Rodolfo Rodríguez Torrens</i>	
Emergency Myocardial Revascularization in Preinfarction Angina	56
<i>George G. Rowe, George M. Kroncke and William P. Young</i>	
Design for Old Living. Advice on How to Better Live with It	61
<i>Rafael Rodríguez Molina</i>	
Editorial: Current Trends in Cataract Extractions	62
<i>José A. Berrocal</i>	
Noticias	63
Abril:	
A 5 Year Double Blind Controlled Clinical Trial of D-Thyroxine on Euthyroid Coronary Subjects - Final Report	64
<i>Elí A. Ramírez, P. H. García Pont and Frankie Alvarado Norat</i>	
En Torno a la Fiebre Reumática	74
<i>Felipe Vizcarrondo y Amalia Martínez Picó</i>	
The Toxicology of Aspirin	78
<i>Sidney Kaye</i>	
Effectiveness of Minocycline in Bacterial Infection	81
<i>Lillian Conde Pérez</i>	
Editorial: Utilization, Nuisance or Necessity?	84
<i>Walter Kleis</i>	
Carta a la Redacción	86
<i>J. Rodríguez Pastor</i>	
Noticias	87
Mayo:	
Takayasu's Arteritis in Pregnancy	90
<i>Francisco X. Veray, Ryan P. Crenshaw, Waldo López, Jorge Gandía, Raúl Yordán and Iván Pelegrina</i>	
Acute Trifascicular Block - A Report of Four Cases and a Review of the Literature	103
<i>Pablo Iván Altieri and Charles Johnson</i>	
Hyperlipoproteinemic Types Among Puerto Ricans: A Progress Report	111
<i>Marta Cancio and José M. León</i>	
Prevention of Complicating Emotional Problems of the Paraplegic	119
<i>Herman J. Flax</i>	

Editorial	122
<i>Emilio Torres Reyes</i>	
Noticias	124
Junio:	
Nueva Operación Para Atresia Tricuspídea, Pulmonar y Condiciones Asociadas con Malformación del Ventrículo Derecho. II. Aspectos Hemodinámicos y Radiológicos	126
<i>Jorge O. Just Viera, Ernesto Rivé Mora, Pablo Iván Altieri, Carlos Girod, Olga L. Rodríguez, Jorge Haddock, Carlos Méndez Bryan y Waldo López</i>	
Comparison of Two Vectorcardiographic Leadsystems (Burger and Frank)	133
<i>Pieter Van Loon, Amalia Martínez Picó, Agustín Muñoz Santiago, Charles D. Johnson and Carlos Girod</i>	
Conceptos Actuales Sobre la Endocarditis Infecciosa	141
<i>Jorge Sánchez, Felipe Vizcarrondo, Enrique Marquez y Amalia Martínez Picó</i>	
Cardiopatía Congénita Severa del Recién Nacido	147
<i>Jorge Sánchez, Georgina Marroig, Ofelia Rojas y Amalia Martínez Picó</i>	
Relaciones Anatómicas Entre la Válvula Pulmonar y la Base de la Orejuela Derecha	157
<i>Renán A. Dieppa y Jorge O. Just Viera</i>	
Editoriales: Hexaclorofeno	159
<i>Mercedes Vega Vidal</i>	
Obsolete Excuses or Obsolete Facilities?	
<i>Héctor L. Rodríguez Fernández</i>	
Noticias	162
Julio:	
The Dextrocardias. A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects (First Part)	165
<i>Charles D. Johnson</i>	
Multiple Sclerosis in Puerto Rico (Experience at the University Hospital) I. Review of a Series of Cases	176
<i>L. P. Sánchez Longo, Miguel Fiol and Pedro Cedó</i>	
The Management of Acute Scrotal Swelling in Children and Young Adults	179
<i>Roberto F. Fortuño and Luis Nieves Valle</i>	
Ley que Regula la Práctica de la Medicina en Puerto Rico - Ley Núm. 22	183
Cartas a la Redacción	190
<i>Francisco Jaime Anselmi</i>	
<i>Pablo I. Altieri</i>	
<i>Ismael Rodríguez Ibáñez</i>	
Noticias	193

Agosto:

The Dextrocardias. A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects (Second Part)	195
<i>Charles D. Johnson</i>	
Cryptococcus Neoformans: Their Identification in Body Fluids and Cultures by Mucicarmine Stain (Mayer)	203
<i>J. F. López and R. Figueroa Lebrón</i>	
Vectocardiografía Cuantitativa en la Unidad de Cuidado Coronario	206
<i>F. Olazábal, Jr., J. Oms y R. Rodríguez</i>	
Post Graduate Medicine in Puerto Rico. A Refresher Course	211
<i>Egidio S. Colón Rivera</i>	
Noticias	218

Septiembre:

Conferencia Magistral "Dr. Ramón J. Sifre" - El Tratamiento de las Complicaciones de la Cirrosis Hepática Avanzada	219
<i>Henry J. Tumen</i>	
El Antígeno Australiano: Características y Significado Clínico	229
<i>Ibrahim Pérez</i>	
Cirugía Radical para Trauma Severo del Hígado y Pulmón	234
<i>Jorge O. Just Viera, José I. Iglesias, F. E. Oliveras Armstrong, Pablo L. Morales y José Raúl González Giusti</i>	
Hepatitis Viral: Conceptos Actuales Sobre Etiología y el Antígeno Asociado a Hepatitis (Australiano)	238
<i>Juan T. Tomasini y Carlos Bañón</i>	
Hyperbilirubinemia Not Due to Hemolytic Disease of Newborn	243
<i>Eloísa Muñoz Dones de Carrascal</i>	
Actualidades Médicas	249
(Abstractos de la Convención Anual de la Asociación Puertorriqueña del Corazón)	
Noticias	253

Octubre:

Programa Asamblea Anual AMPR	256
Resúmenes de Trabajos Presentados en el Programa Científico	270
Treatment of Drug Resistant Hypertension in Chronic Kidney Disease	279
<i>José L. Cangiano, Rafael Ramírez González, Osvaldo Ramírez Muxó, Enrique Pijem and Elaine Waddell</i>	

Editorial: Programa Control de Enfermedades Venéreas: Función y Objetivos	283
Actualidades Médicas	284
(Criteria and Techniques for the Diagnosis of Gonorrhea. Resumen de las Recomendaciones del Comité Asesor sobre Terapéutica - Centro de Control de Enfermedades, Atlanta, Ga.)	
Noticias	289
Noviembre:	
Histoplasmosis Aguda - Epidemia en San Germán	291
<i>Rafael Díaz Martínez</i>	
Gentamicin: A Clinical Study	295
<i>Roberto F. Fortuño and Rubén Cartagena</i>	
Fiebre Reumática Activa Simulando Apendicitis Aguda	298
<i>Rafael Villavicencio, Jorge Sánchez y Amalia Martínez Picó</i>	
Dihydrogenated Alkaloids of Ergot in Geriatric Patients: Symptomatic Treatment of Cerebrovascular Insufficiency	301
<i>C. Kaye</i>	
Sección de Libros	304
<i>A. Rodríguez Olleros</i>	
Noticias	305
Diciembre:	
Long Term Results of Intermittent Steroid Treatment in the Adult Nephrotic Syndrome	308
<i>José L. Cangiano, Rafael Ramírez González, Arturo Trevino, Rosa Lluberes, Jesús Vázquez, Rodrigo Menéndez Corrada and Osvaldo Ramírez Muxó</i>	
Patrón de Selectividad de Proteínas en Enfermedades Renales	314
<i>Rosa Lluberes, Arturo Trevino, José L. Cangiano, Osvaldo Ramírez Muxó, Rafael Ramírez González y Rodrigo Menéndez Corrada</i>	
Prueba de Excreción Urinaria de Xilosa: Utilidad y Limitaciones en la Separación de Niños Normales de Pacientes con Esprú Tropical	319
<i>Pedro J. Santiago Borrero, Rafael Santini, Jr., Irma Ramírez y Norman Maldonado</i>	
Discurso: La Profesión Médica ante los Cambios que se Avecinan	323
<i>Félix S. Vilella Suau</i>	
Editorial: Acción y Reflexión	325
<i>José M. Rigau</i>	
Nota Biográfica: Dr. José M. Rigau Marqués	328
Contenido - Volumen 64	332
Índice de Autores	337
Índice de Materias	340

Altieri, Pablo Iván	103, 126, 190
Alvarado Norat, Frankie	64
Arraut, Edda Torres de	23
Bañón, Carlos	238
Berrocal, José A.	62
Burgos Calderón, Rafael	1
Cancio, Marta	111
Cangiano, José L.	14, 279, 308, 314
Carrascal, Eloísa Muñoz Dones de	243
Cartagena, Rubén	295
Cedó, Pedro	176
Colón Rivera, Egidio S.	211
Conde Pérez, Lillian	81
Crenshaw, Ryan P.	90
Díaz Martínez, Rafael	291
Dieppa, Renán A.	157
Figuroa, Julio E.	1
Figuroa Lebrón, R.	203
Fiol, Miguel	176
Flax, Herman J.	119
Fortuño, Roberto F.	179, 295
Fox, Irving	53
Gandía, Jorge	90
García Castro, José Miguel	8
García Pont, P. H.	64
Girod, Carlos	126, 133
González Giusti, José Raúl	234
Haddock, Jorge	126
Hernández Morales, Federico	5
Iglesias, José I.	234
Jaume Anselmi, Francisco	190
Johnson, Charles	103, 133, 165
Just Viera, Jorge O.	39, 44, 126, 157, 234

Kaye, Carmen	301
Kaye, Sidney	78
Kleis, Walter	84
Kroncke, George M.	56
León, José M.	111
Lergier, Julio E.	48
Lluberes, Rosa	308, 314
López, J. F.	203
López, Waldo	90, 126
Maldonado, Norman	319
Marquez, Enrique	141
Marroig, Georgina	147
Martínez Picó, Amalia	17, 23, 39, 74, 133, 141, 147, 298
Méndez Bryan, Carlos	126
Menéndez Corrada, Rodrigo	308, 314
Morales, Pablo L.	234
Muñoz, Agustín	23, 133
Nieves Valle, Luis	179
Olazábal Jr., F.	206
Oliver González, José	5
Oliveras Armstrong, F. E.	234
Oms, J.	206
Pelegrina, Iván	90
Pérez, Ibrahim	229
Pérez Comas, Adolfo	8
Pijem, Enrique	279
Ramírez, Elí A.	64
Ramírez, Irma	319
Ramírez González, Rafael	279, 308, 314
Ramírez Muxó, Osvaldo	279, 308, 314
Rigau, José M.	325, 328
Rivé Mora, Ernesto	44, 126
Rodríguez, Olga	44, 126
Rodríguez, R.	206
Rodríguez Fernández, Héctor L.	159
Rodríguez Ibáñez, Ismael	191
Rodríguez Molina, Rafael	61
Rodríguez Olleros, A.	304
Rodríguez Pastor, J.	86
Rodríguez Torrens, Rodolfo	53
Rojas, Ofelia	147
Rowe, George G.	56

Sánchez, Jorge	17, 141, 147, 298
Sánchez Longo, L. P.	176
Santiago Borrero, Pedro J.	319
Santini Jr., Rafael	319
Tomasini, Juan T.	238
Torres Reyes, Emilio	122
Trevino, Arturo	308, 314
Van Loon, Pieter	133
Vázquez, Jesús	308
Vega Vidal, Mercedes	31, 159
Veray, Francisco X.	90
Vilella Suau, Félix S.	323
Villavicencio, Rafael	17, 298
Vizcarrondo, Felipe	74, 141
Waddell, Elaine	279
Yordán, Raúl	90
Young, William P.	56

Actualidades Médicas	249, 284
Acute Oliguric Renal Failure Associated with Low-Molecular-Weight Dextran	1
Acute Scrotal Swelling in Children and Young Adults, The Management of	179
Acute Trifascicular Block - A Report of Four Cases and a Review of the Literature	103
Antígeno Australiano, El: Características y Significado Clínico	229
Asamblea Anual AMPR, Programa	256
Atresia Tricuspídea, Pulmonar y Condiciones Asociadas con Malformación del Ventrículo Derecho. I. Aspectos Quirúrgicos, Nueva Operación Para	44
Atresia Tricuspídea, Pulmonar y Condiciones Asociadas con Malformación del Ventrículo Derecho. II. Aspectos Hemodinámicos y Radiológicos, Nueva Operación Para	126
Cardiopatía Congénita Severa del Recién Nacido	147
Cartas a la Redacción	86, 190
Cirrosis Hepática Avanzada, El Tratamiento de las Complicaciones de la - Conferencia Magistral "Dr. Ramón J. Sifre"	219
Constricción Quirúrgica de la Arteria Pulmonar: Experiencia en 80 Casos	23
Contenido - Volumen 64	332
Cryptococcus Neoformans: Their Identification in Body Fluids and Cultures by Mucicarmine Stain (Mayer)	203
Dextrocardias, The: A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects (First Part)	165
Dextrocardias, The: A Review and a Report of 26 Cases, Emphasizing Electrocardiographic and Vectorcardiographic Aspects (Second Part)	195
Dihydrogenated Alkaloids of Ergot in Geriatric Patients: Symptomatic Treatment of Cerebrovascular Insufficiency	301
Discurso: La Profesión Médica ante los Cambios que se Avecinan	323
Drug Resistant Hypertension in Chronic Kidney Disease, Treatment of	279
D-Thyroxine on Euthyroid Coronary Subjects, A 5 Year Double Blind Controlled Clinical Trial of, - Final Report	64
Editoriales:	
Dextran 40 - Paradox of Treatment	14
Cardiología Pediátrica: Alcances en Puerto Rico	39
Ejemplo, Problemas y Preguntas	
Current Trends in Cataract Extractions	62
Utilization, Nuisance or Necessity?	84
Sin Título	122
Hexaclorofeno	
Obsolete Excuses or Obsolete Facilities?	159
Programa Control de Enfermedades Venéreas: Función y Objetivos	283

Acción y Reflexión	325
Endocarditis Infecciosa, Conceptos Actuales Sobre la	141
Excreción Urinaria de Xilosa, Prueba de: Utilidad y Limitaciones en la Separación de Niños Normales de Pacientes con Esprú Tropical	319
Fiebre Reumática Activa Simulando Apendicitis Aguda	298
Fiebre Reumática, En Torno a la	74
Gentamicin: A Clinical Study	295
Hepatitis Viral: Conceptos Actuales Sobre Etiología y el Antígeno Asociado a Hepatitis (Australiano)	238
Histoplasmosis Aguda - Epidemia en San Germán	291
Hyperbilirubinemia Not Due to Hemolytic Disease of Newborn	243
Hyperlipoproteinemic Types Among Puerto Ricans: A Progress Report	111
Immunosuppressive Therapy - Basic Concepts and Recent Advances	48
Impresiones Dermopapilares: Dermatoglíficos y Surcos de Flexión. I. Conceptos Básicos	8
Índice de Autores	337
Índice de Materias	340
Intermittent Steroid Treatment in the Adult Nephrotic Syndrome, Long Term Results of	308
Ley que Regula la Práctica de la Medicina en Puerto Rico - Ley Núm. 22	183
Macellaria Myiasis in Puerto Rico, Human	53
Marcapasos en Niños: Diez Años de Experiencia Clínica	31
Minocycline in Bacterial Infection, Effectiveness of	81
Myocardial Revascularization in Preinfarction Angina, Emergency	56
Nota Biográfica - Dr. José M. Rigan Marqués	328
Noticias	15, 41, 63, 87, 124, 162, 193, 218, 253, 289, 305
Old Living, Design for. Advice on How to Better Live With It	61
Paraplegic, Prevention of Complicating Emotional Problems of the	119
Post Graduate Medicine in Puerto Rico. A Refresher Course	211
Proteínas en Enfermedades Renales, Patrón de Selectividad de	314
Resúmenes de Trabajos Presentados en el Programa Científico	270
Schistosomiasis Mansoni in Adults with Sodium Dimethylcysteine Tartrate, Treatment of	5
Sclerosis in Puerto Rico, Multiple (Experience at the University Hospital) I. Review of a Series of Cases	176
Sección de Libros	304
Takayasu's Arteritis in Pregnancy	90
Tetralogía de Fallot: Conceptos Actuales de su Tratamiento	17
Toxicology of Aspirin, The	78
Trauma Severo del Hígado y Pulmón, Cirugía Radical para	234
Válvula Pulmonar y la Base de la Orejuela Derecha, Relaciones Anatómicas Entre la	157
Vectocardiografía Cuantitativa en la Unidad de Cuidado Coronario	206
Vectoreardiographic Leadsystems (Burger and Frank), Comparison of Two	133

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